

The New England Journal of Medicine

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VOLUME 221

OCTOBER 5, 1939

NUMBER 14

THE SOCIAL AND ECONOMIC SITUATION OF THE, MEDICAL PROFESSION IN SWEDEN

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UPSALA SWEDEN

THE social and economic situation of the members of the medical profession in Sweden may be said to be good, even admitting certain disadvantages connected with the present system of university education and early post graduate work in the hospitals. The time devoted to studies is too long according to most authorities, and a plan for reform is at present under discussion in the faculties of medicine. The final examination (Licentiate of Medicine) is usually reached after eight, nine or sometimes more years of medical study. The time before the examination is divided into two parts. The first is purely theoretical and takes about three years. During the second part the students work in all the different departments of a hospital and there is no specialization during this time. Even after this training it is practically impossible for the young doctor to get a situation which will enable him to earn a living. Work as assistant in a hospital without any salary for about a year is almost always necessary in order to get a paid position on the staff of a hospital. This corresponds to the so-called "practical year" in other countries.

Medical education is very expensive, and even though the state pays for practically all the teaching, the students are usually heavily in debt before being able to earn a living. At present there are very few scholarships available, however, it now looks as if the Government had under consideration a plan to increase them.

Of late there has been a growing tendency among the members of the profession to continue their studies after the final examination in order to obtain the degree of Doctor of Medicine. In the five year period 1908-1913 32 obtained the advanced degree. In the period 1929-1934 the corresponding figure was 48. There has thus been

an increase of 50 per cent in the number who have continued with scientific work. This is to be regarded as a sign of increased interest, but in addition, the degree of Doctor of Medicine adds to the stated number of credits which carry weight when applying for a position.

It is pointed out above that there exist very few scholarships and that most of the students are heavily in debt before being able to earn a living. The present tendency to produce a thesis, when the author has no intention to continue in an academic career, naturally increases very considerably the sum needed for a medical education. The experimental and clinical work entailed necessitates a long period of time for this study (from one to several years). Moreover, the cost of publication is usually paid by the author. It is the custom to publish a thorough report based on the clinical, chemical or other original data used in the discussion of the topic. Thus, a thesis for the degree of Doctor of Medicine usually comprises two hundred to three hundred or more pages.

After the first postgraduate year in a hospital it is usual to apply for a position as assistant on the staff of one of the large communal or provincial hospitals. The private hospitals are few and of no importance for postgraduate training, although it is true that they exist in some of the large communities and are to a greater or lesser extent self-supporting or rely on private funds and donations. During the first years as assistant in a public hospital the salary is usually very low, and the fact that the assistants are obliged to eat and live in the hospitals imposes a rather modest standard of living. Since these appointments are regarded as necessary to obtain a good position later on, there are always applicants, and the provincial authorities have sometimes shown very little interest in improving the working conditions. In order to protect their own interests the younger

doctors in Sweden have formed a special association and it appears as if its importance would rapidly increase

An appointment as first assistant in one of the large hospitals usually is relatively sound economically, and this may be said as well of the positions of chief physician and surgeon. These men are appointed by the Central Medical Board of Sweden and the Government, and after reaching the age of sixty-five they enjoy a pension from the state. The procedure for their selection is rather complicated, and as competition for these places is becoming increasingly keen it is very unusual to obtain these positions before the age of forty.

This method of appointment is certainly not an advantage for the parties concerned. The chief qualification involves many years as assistant in different hospitals and especially in the university clinics. Of late the degree of Doctor of Medicine has become an almost indispensable requirement. The chiefs of the different clinics of a hospital, however, are very well situated. They receive a salary from the authority in charge of the hospital. In addition they are allowed to see private patients in the hospital and to charge fees for their treatment. In this respect they may be compared to the consulting surgeons and physicians in other countries. Many of their cases are sent to them by colleagues. On the other hand, they are not supposed to have a large consulting practice in the town or province and their work is almost entirely devoted to their hospitals. As they spend practically their whole time in the hospital they may well be regarded as having a full-time post. This is certainly one of the most important features of the Swedish medical organization.

The treatment in practically all the public hospitals is free or extremely cheap, and the costs are paid not by charitable funds or gifts but by the local authorities through taxation. If a patient has no means of paying for himself, the community to which he belongs pays his fee through the poor-law system. The majority of patients, however, pay from 1.00 to 1.25 crowns (25 to 30 cents) a day. In this fee all sorts of examinations (microscopical, chemical, radiological) and all types of treatment, even the costs of operations, are included. No fee is paid to the doctor. Patients with a somewhat higher yearly income pay 2 to 4 crowns (50 cents to 1 dollar) a day.

If a patient wishes to be treated in a private ward with one or two persons in each room and to receive other extra facilities, the fee is considerably higher, 10 to 15 crowns (2 to 4 dollars) a day. These private wards represent a section of the public hospitals, and were built and are managed by the authority that owns the hospital.

All fees revert to the hospitals, with the exception of the special honorariums paid by the private patients to the chief surgeon or physician of the wards and to the consulted specialists. They are as a rule fixed according to a scale of charges approved by the authorities. Such payments are extremely modest when compared to those of most other countries, and medical care cannot be regarded as a very heavy economic burden in Sweden. It is proper to add, however, that the economic situation of a chief of a hospital in Sweden is very good.

During the last decade another division of hospital work, namely the outpatient department (polyclinic), has gained considerably in importance, chiefly as a result of the dominating position of the different technical devices for the diagnosis of disease. There seems to be a very strong tendency among such patients to overestimate the importance of procedures such as an x-ray examination, and it is an everyday experience for patients to demand an x-ray, for example of the head, in the most various, and usually functional, disorders. A colleague of mine, who was then chief of an outpatient department, used to say that he spent much of his time trying to convince the patients that this department of the hospital was not a "photographer's studio." It is not easy to say whether the further development of the polyclinic is to be a happy one or not. In regular outpatient departments the patients only pay 2 to 4 crowns (50 cents to 1 dollar) for a consultation. The fee goes to the hospital,* and the assistants are paid a monthly salary regardless of the amount of work they are obliged to perform. This system of payment has many advantages and a few disadvantages. Both doctor and patient have the feeling that everything that is done has a real meaning for the investigation of the case, and the patient is less apt to feel himself neglected if little can be done, or unjustly charged if there are many complicated examinations. If the salary of the assistants is sufficient, everything is all right, but it seems obvious that the present system may lead to abuses from the authorities in the form of demanding much work for little pay.

As the hospitals are all, with a few exceptions, managed either by the province or the town, they are regarded as belonging to the inhabitants of that district. Patients coming from other parts are admitted but are charged a higher fee.

Many far-sighted medical men regard the large-scale development of polyclinics with some misgiving. The treatment in a big hospital with a large number of patients for each doctor always

*In some communities the assistants receive the honorarium paid by the patient.

tends to be somewhat mechanical. It is clear, on the other hand, that it is the function of a hospital to treat patients with major infirmities from the very start, and thereby the patients should receive better treatment than they could secure from their family doctor. But with this system the large group of minor illnesses cost the community large sums every year, and the patients would probably feel much happier if they were treated at home or in their own village by their own doctor. My impression is, therefore, that the polyclinics ought not to be increased on a very large scale and that the co-operation between the general practitioner and the hospital should be developed as much as possible.

There are, however, several conditions in which the hospitals ought to have a monopoly in the treatment of patients. I refer to diabetes mellitus, pernicious anemia and naturally also such minor surgical injuries as need x-ray examination, for example fractures.

In Upsala we have tried to form a sort of dispensary for the cases with diabetes and pernicious anemia, and to some extent also for the patients with essential hypochromic anemia (iron deficiency anemia). The regular supervision of these patients is indispensable and in order to keep the patients under control a system of free medication has been instituted. The patients pay only the ordinary fee for a consultation. The necessary laboratory examinations are performed and the diabetic patient is given a prescription for a certain amount of insulin. He is entitled to this amount from the hospital either without any payment or at a much reduced price, depending on his economic position. In this way he has also an economic interest in coming back to the polyclinic before his insulin is quite finished in order to obtain a new supply and his status is then controlled. The system appears to work very well. The same may be said of the treatment of pernicious anemia. No other treatment but injection of a really potent liver extract is used. The patients usually get 10 cc every four six or eight weeks, according to their need. The condition of the blood is controlled every time, and the treatment adjusted if there seems to be need for it. No extra charge is made for medication and all the patient must do is to come to the hospital six or ten times a year to get his injections. With a card index system the regular return of the patient may be checked and he is reminded by letter of his promise to come back if he is shirking. This system appears to work admirably, and it is certainly less expensive even for the hospital than to let the patients come back with severe relapses of anemia, advanced subacute com-

bined degeneration of the spinal cord or diabetic coma. As a matter of fact, none of these complications are now seen among our regular patients in Upsala.

Throughout the country there are also special outpatient departments for those suffering from tuberculosis of the lungs and for their relatives and the contacts for whom examination is gratuitous. The dispensary organization for the detection of early infective cases of tuberculosis and for their isolation works well. In every province there is a central sanatorium and each has a chief physician who devotes all his time to the hospital. Most cases of severe tuberculosis of the lungs are sent to him in order that he may give his opinion on the case and start the treatment. Many patients are treated in small sanatoriums in their own districts but are always under medical supervision. There is a very effective system of dispensaries with doctors and nurses for the control of patients after their cure in a sanatorium and for the following of sanitary conditions in homes, especially among the children.

Treatment for venereal disease in a contagious stage is free and paid by the state according to the Swedish law for the prevention of venereal disease. As this law has apparently been discussed on several occasions in the United States I shall not enter into this question here.

All the asylums for mental diseases are conducted by the state or by the big cities. The formalities necessary for admission are very complicated in order to render unjustified confinements more difficult. The individual is thus well protected under the present regulations but the result is that the system is rather inflexible.

For the care of the crippled there is an orthopedic hospital in Stockholm and several in the country with schools for the children and shops for adults where the patients may learn a suitable craft. The hospital is supported by the Government and by private funds. All the traveling expenses of the patients from any part of Sweden are paid by the hospital and a very considerable part or the whole of the sum necessary for bandages is also furnished without charge.

Another organization with a central hospital in Stockholm which treats cases from the whole country is the cancer hospital (*Radium Hemmet*). It was first started with private means but has now a grant from the state and a large endowment formed from the nation's gift to the King on the occasion of his seventieth birthday. Most of the radium treatment in Sweden is centralized here, and the patients travel to it at the expense of the hospital. The further development of cases

is studied most thoroughly, and a very comprehensive card index of the patients, their treatment, their visits to the hospital after different periods of time and so on has been established

The most important part of the medical work outside the hospital is done by the public-health officers. They are appointed by the Government and their hospital training has usually been very thorough (ten years or more). The public-health officer has the control of the sanitary conditions in his district and is obliged to report to the authorities on epidemiological and hygienic questions. But he is also a general medical practitioner. He receives a salary from the state and when retiring at sixty-seven is given a pension. The poor people in the district get their treatment without any payment, the others pay according to a scale of charges approved by the Government. It is very usual for the public-health officer to be medical adviser to the schools and to the railway personnel in his district, and most of the officers enjoy an excellent economic situation. In many districts they have small hospitals for their own use where they are able to perform appendectomies and most minor operations. It is also common in small districts for them to have sanatoriums under their supervision which collaborate with the central provincial sanatorium for pulmonary tuberculosis.

As may easily be inferred from the facts mentioned above, the importance of the general practitioner is considerably less than in most other countries. There is also little use for a system with consulting surgeons and physicians in a country with long journeys between patients. When a public-health officer or practitioner in a town wishes to consult a colleague he usually sends the patient to the wards or to a private room in the hospital. A patient with a letter from a practitioner in the province is usually admitted to the wards without much delay.

The last examination (Licentiate of Medicine) gives the formal right to practice medicine, but the usual procedure is to secure a training in a hospital for several years in order to get the competence necessary for a specialist. As a rule, general practitioners and specialists are found only in the important municipalities, and all the medical work in the rural districts and a great

part of that in small cities are carried out by medical men appointed by the Government. It is thus socialized to a certain degree. The present system seems to work very well, and is certainly popular both among the public and the members of the profession.

There are a few general arrangements for public welfare that play a great part in the medical life of the country. One is the governmental pension system for the disabled. If a person suffers from a chronic disease to such extent that his working capacity for the future must be regarded as less than one third of normal, his physician may fill out a form, and if the claims are acknowledged by the Central Board of Pensions, the patient receives a small pension for the rest of his life. This system has on the whole been very successful, but it is obvious that many disputes arise concerning the question of what is less than one third of normal working capacity. The necessity for the doctor not only to help his patient but also to be a judge of the justice of his claims is increasing steadily. My personal impression is that this may lead to a serious conflict not only as regards pensions, but also in other economic matters connected with ill health. There has been an increasing tendency in some parts of the administration of the law to assign to the profession a position equivalent to that of a judge, which certainly ought to be opposed. Our chief aim should always be to cure patients and not to supervise them and act as policemen.

Considerable discussion has arisen of late about the most suitable medical system for the provident societies. Among the medical associations there seemed to be an almost unanimous opinion that a system with only one approved doctor for each society must be avoided. It was regarded as most important that the choice of doctor be left to the patient, and this is the form now in practice. As there is no compulsion to belong to provident societies their importance varies in different provinces. They provide for medical care, medicine and a certain daily payment during the time of illness. As a matter of fact, insurance for accidents during work is compulsory for an employer, and certain occupational diseases are also regarded as belonging to the same group. Swedish legislation presents no special features in this respect.

PIGMENT EXCRETION IN PELLAGRA*

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THE presence of increased amounts of porphyrin in the urine of pellagrins was first reported by Beckh, Ellinger and Spies.¹ This paper was based on a study of 14 cases of alcoholic pellagra, and 1 case associated with tuberculous enteritis. A simple test (referred to in this communication as the "B.E.S. test") was employed for the detection of porphyrin in the urine. It has since been shown, however, that the B.E.S. test is not specific for porphyrin,² since positive results are mainly due to some other pigment or pigments, which Spies and his associates³ now call "porphyrin-like substances." Dobriner and his collaborators⁴ and Watson⁵ have subsequently shown that porphyrin in increased amounts may occur in the urine of alcoholic pellagrins. Since, however, porphyrinuria is known to occur in various diseases accompanied by liver disorder, it is possible that the porphyrinuria of alcoholic pellagra may be due to the effects of alcohol on the liver, rather than to the associated vitamin deficiency. It was decided, therefore, to investigate the pigment excretion in endemic pellagra unassociated with alcoholism.

Twenty-four hour specimens of urine from 4 cases of endemic pellagra were obtained through the kindness of Dr. Tom D. Spies. He reported to us that these were all mild cases without dermatitis or psychosis. Two patients had previously received nicotinic acid therapy which had not been completely curative and which had been stopped a few weeks prior to the collection of the specimens. The specimens were sent from Birmingham, Alabama, to Boston under toluene, and were examined for ether-soluble porphyrin, one to two weeks after collection, by a modification of the quantitative fluorometric method of Brugsch.⁶ In none of the specimens examined was it possible to demonstrate any unusual amount of coproporphyrin. No definite conclusion can be drawn from this finding so far as porphyrinuria in endemic pellagra is concerned, since the patients from whom the specimens were obtained did not suffer from severe pellagra, and furthermore it

is possible that porphyrin present in the fresh urine may have decomposed in transit. Some of the specimens, however, gave a positive B.E.S. test.

The B.E.S. test essentially consists of preparing an acetic acid and ether extract of urine and extracting the ether with 25 per cent hydrochloric acid.⁷ The appearance of a pink color in the hydrochloric acid layer is considered by Spies as a positive test for porphyrin-like substances.⁸ Watson⁵ was able to demonstrate that the ether extract of urine from 3 cases of alcoholic pellagra contained a red pigment which possessed some of the characteristics of indirubin. In only 1 case, however, was he able to extract any red pigment from the ether by means of 25 per cent hydrochloric acid. This suggests that indirubin, the pigment described by him, is not the pigment responsible for the B.E.S. test. Moreover, it is improbable that indirubin could be the pigment, since indirubin is soluble in ether but insoluble in aqueous solutions, and, therefore, would not be extractable from ether by 25 per cent hydrochloric acid. However, Watson's experiments have drawn attention to the possibility that the pigment obtained in the B.E.S. test may be some other derivative of indol. The following observations are concerned with an investigation of this possibility.

While this work was being prepared for publication Watson⁵ independently had extended his investigations on this problem, and he has shown that, in addition to indirubin, a pigment resembling urochrome is formed by the action of hydrochloric acid on etheral extracts of urine obtained from patients suffering with various diseases, including pellagra.

Urine specimens from 3 of Dr. Spies's cases of endemic pellagra were found to exhibit an unusual reaction to carrying out Jaffe's test for indican⁹; it was found that a positive test was obtained immediately following the addition of acid, without the usual need for an oxidizing agent. After extracting the indigo blue with chloroform, another pigment, cherry red in color, was ex-

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The expenses of this investigation were defrayed in part by a gift to Harvard University from Eli Lilly and Company, Indianapolis, Indiana.

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This term is used in the sense employed by other authors, namely 1 part of concentrated hydrochloric acid solution in 3 parts of water of approximately 9 per cent free acid.

§) If a test is carried out by adding to the urine an equal volume of concentrated hydrochloric acid and a few drops of calcium hypochlorite solution, an indigo blue pigment is oxidized to indigo blue, which is extracted with chloroform.

tracted with amyl alcohol. This is customarily known as the urochrome reaction.

The presence of indican in the urine of pellagrins has been recorded previously,^{8, 9} but no reference has been found to the occurrence in pellagrous urine of this direct indican reaction (a positive reaction in the absence of added oxidizing agent). However, direct indican and urochrome reactions have been reported in other pathologic conditions. Herten¹⁰ attributed such reactions to bacterial decomposition of the urine, but Ross¹¹ showed that a direct urochrome reaction may be given by freshly passed urine. In the course of the present investigation urine specimens from 100 patients selected at random have been tested for indican. Direct indican reactions were observed in specimens from 15 patients suffering from a variety of diseases.* Specimens giving this reaction also showed a positive B.E.S. test. In some cases a direct indican reaction was not obtained when the urine was first passed, but developed after the urine had been allowed to stand. This, however, was not due to bacterial action, since fresh specimens maintained in a sterile condition after Berkefeld filtration showed the same phenomenon.

These observations suggest that urine specimens which give a positive reaction for indican in the absence of added oxidizing agent contain some abnormal agent capable of oxidizing indol derivatives in the presence of strong acid. Since the unoxidized indol derivatives which may occur in the urine are all soluble in ether, the oxidation of these derivatives might take place under the conditions of the B.E.S. test, if the abnormal oxidizing agent were also ether-soluble. The following results demonstrate that this apparently is the explanation of a positive B.E.S. test.

Specimens of urine from 2 of Dr. Spies's cases and from 3 non-pellagrous patients, all exhibiting a positive B.E.S. test, were studied. The B.E.S. test was carried out on 50-cc. samples of urine as follows: The sample was brought to pH 4 with glacial acetic acid and extracted with twice its volume of ether. The ether layer, which showed no trace of red coloration, was washed twice with water and extracted with small amounts of 25 per cent hydrochloric acid. A pink pigment appeared in the hydrochloric acid extracts, and the extraction was repeated until no more color was obtained. After the extracted ether had been allowed to stand for twelve hours over 25 per cent hydrochloric acid a second yield of pigment was obtained, and was found to have the same properties as the first. The pigment could

not be extracted from the 25 per cent hydrochloric acid solution by chloroform or benzene but was readily extracted by amyl alcohol. The amyl alcohol solution slowly changed color on exposure to light, becoming red-brown instead of pink. On the addition of excess alkali the hydrochloric acid solution turned brownish yellow, but when the solution was again made acid the pink color was restored. Spectroanalysis of the amyl alcohol solutions showed two absorption bands with maxima in the vicinity of wave lengths of 500 and 530 millimicrons respectively, together with a general reduction in transmission at the violet end of the spectrum (Fig. 1). In the case of the

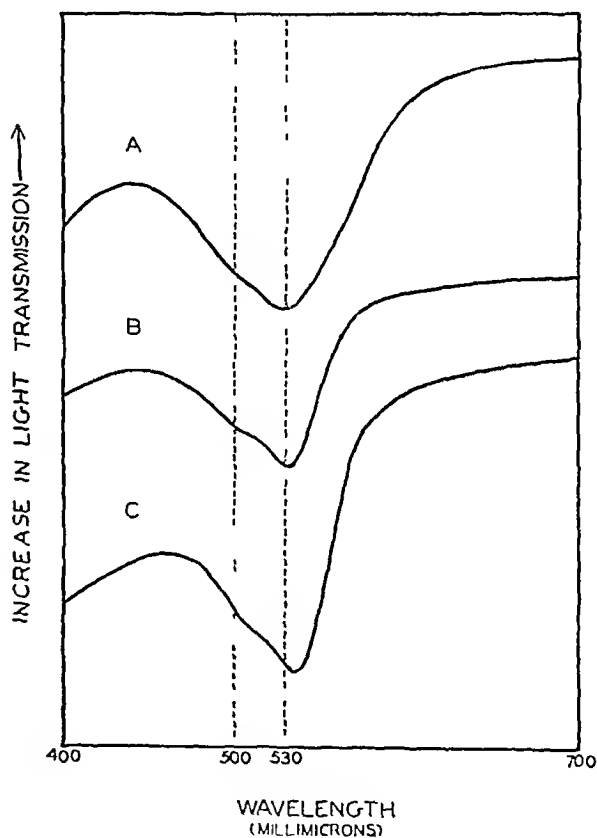


FIGURE 1

Spectro-analysis of the B.E.S. pigment derived from the urine of 2 cases of endemic pellagra (A and B), and of the pigment obtained from the oxidation of indol-acetic acid (C), showing the position of their absorption bands. These records were obtained with an automatic recording spectrograph.

pigments derived from the pellagrous urines the band at 500 millimicrons was very faint, in the other 3 cases this band was more prominent. In each case the change of color which took place on exposure to light was accompanied by disappearance of the characteristic absorption spectrum.

In all these properties the B.E.S. pigment closely resembles those pigments which have been de-

*The possibility that these direct reactions are partly due to some oxidizing agent present as an impurity in the hydrochloric acid has been investigated. No such impurity could be detected by means of potassium iodide and starch solutions.

scribed very frequently in the past is occurring in urines from diseased subjects and have been variously named uro-roscin, nephro-roscin and skatol red. The properties described as characteristic of these three pigments are essentially similar, although reports of minor differences in solubility and spectral characteristics have led some to conclude that they are not identical. Their chemical nature does not appear to have been determined although as Herter¹² showed the pigment derived from the oxidation of indolacetic acid has the same properties as those ascribed to uro-roscin. It would seem highly probable that these pigments are mixtures of several closely related chemical entities, and may be derived from the oxidation of more than one compound of indol. This might account for the minor differences in the early description of these pigments.

Since uro-roscin has been described as being identical with the pigments obtained by the oxidation of indolacetic acid a comparison was made between oxidized indolacetic acid and the B.E.S. pigment. Indolacetic acid* in aqueous solution was treated in the presence of an equal volume of concentrated hydrochloric acid by the addition of potassium nitrite. The pigment so formed was magenta but turned rapidly to a deep cherry red. With one exception, the properties of this red pigment were found to correspond with the properties previously described for the B.E.S. pigment, except that the spectrum showed a minor difference, in that the principal absorption band in the region of 530 millimicrons reached its maximum 5 to 7 millimicrons nearer to the red end of the spectrum (Fig. 1).

SUMMARY

No increase in porphyrinuria was found in 4 cases of endemic pellagra unassociated with alcoholism. This finding however, must await fur-

ther confirmation since the urine samples were shipped from a distance and the porphyrin may have decomposed in transit.

It is concluded that a positive B.E.S. test is due to the oxidation of ether soluble indol derivatives in the presence of hydrochloric acid with the production of pigments giving a characteristic uro-roscin reaction. The pigments responsible for this reaction are insoluble in ether but soluble in water, and would therefore appear in the hydrochloric acid layer. They have spectral lines at 500 and 530 millimicrons.

The presence of substances in the urine of pellagrins capable of giving the uro-roscin reaction confirms the recent investigations of Watson.⁷

As a result of the present investigations and those of Watson it would seem more proper to refer to the B.E.S. test as indicating the presence of pigments capable of producing the uro-roscin reaction rather than to refer to such pigments as porphyrin like substances, which they in no manner resemble.

The nature of the oxidizing agent which is responsible for the unusual ease with which these indol derivatives are oxidized both in ethereal and in aqueous solutions, is being further investigated.

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* Indol and indolacetic acid were supplied through the courtesy of S. H. Kline and French Laboratories, Philadelphia and Merck and Company Incorporated, Rahway, New Jersey.

ALLERGIC REACTION TO INSULIN*

REPORT OF A CASE

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ALLERGIC reactions following injections of crystalline insulin, although reported by a number of observers,¹⁻⁷ are not common. It is conceivable that occasionally they may be the result of sensitivity to the components of the solvent (glycerin) or to the preservative it contains (tricresol or phenol), but usually insulin itself appears to be responsible. This was true in the case to be reported.

REPORT OF CASE

The patient, an undernourished, non-diabetic man 53 years old, who several years previously had been treated with insulin for the purpose of gaining weight, wished to repeat the treatment. In view of the allergic reactions that occurred during this second course of treatment some of the historical data in the case may be important because of their possible allergic implications.

He had suffered from headache since childhood, more severely in recent years. The headache had been migrainous in character, usually unilateral, beginning in the temporo-frontal region with a feeling of severe pressure over the eye, often extending over the entire head and accompanied by nausea. He had had eczema. For a time, treatment with ergotamine tartrate ameliorated the headache, but during the previous few months it had failed to give relief. His mother also had suffered from migraine.

About 7 years previously the patient had taken 5 units of insulin three times a day for the purpose of gaining weight. He gained 16 pounds and felt better in general while he took insulin but stopped the injections after 4 months because of the inconvenience. Thereupon his weight diminished again. He had always been tall and thin; his height was 6 feet 3 inches, his greatest weight was 152 pounds in 1904, the lowest 100 pounds in 1918 after an attack of influenza.

Because of his previous favorable experience with insulin he decided to resort to it again. On July 2, 1938, he began taking 5 units of standard insulin three times a day. Nine days after beginning the treatment large erythematous itching patches of urticaria appeared on the flexor surfaces of the arms and wrists, whereupon the injections were stopped. On the following day the lesions had extended over the entire body, then they gradually faded and were gone 3 days later. The insulin used had been made from pork pancreas. An injection of 5 units of insulin made from beef was then tried. Shortly afterward the patient had a severe chill, a temperature of 101°F, recurrence of generalized urticarial eruption and a sensation of severe substernal pressure and pain which required an injection of morphine for relief. The blood pressure during the attack was 80/60. The treatment was temporarily abandoned, but about 4 months later it was decided to try

crystalline zinc insulin (Stearns), made from beef. Ten minutes after the injection of 5 units there was a burning sensation of the eyes, the eyelids began to swell and looked inflamed, a severe pain and a sense of constriction were felt in the chest, there was a feeling of fullness in the throat, erythematous urticarial wheals appeared all over the body, a chill followed and the blood pressure fell to the same low level as with the previous experience. The reaction was in every way similar to the others, although slightly less severe.

Endermal tests were made with extracts of pork and beef muscle, with solutions of crystalline zinc-insulin and with solutions of glycerin and tricresol. The solutions of the proteins of beef and pork were diluted to contain 0.1 mg. nitrogen per cubic centimeter. The amount injected was 0.01 cc. All the intracutaneous tests, with the exception of that made with insulin, gave negative results. Where the insulin was injected an irregular wheal was produced measuring 23 by 33 mm, with long pseudopodia (Fig. 1). There was marked itching. The wheal



FIGURE 1 *Intradermal Reaction to Insulin*

was surrounded by an erythematous area measuring 65 by 80 mm. In addition to the local reaction there were general symptoms similar to but much less severe than those observed after the injection of the therapeutic amounts.

In a number of published cases of allergic reaction to insulin the sensitivity was transferable to normal skin by injecting it with the patient's serum, according to the technique of Prausnitz-Küstner. The serum of our patient did not contain sensitizing antibodies demonstrable by this passive-transfer technique. This was true also in the cases reported by Grishaw⁸ and by Murphy, Beardwood and Miller.⁹

Rapid desensitization was accomplished by a method similar to that described by Corcoran¹⁰ and others.¹⁰⁻¹² The schedule of the desensitizing injections is shown in Table I. The initial small amounts, beginning with 0.01 cc. (0.4 units), were given intracutaneously and elicited minor local reactions, the later subcutaneous injections

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tions did not. The amounts were increased rapidly to 0.2 cc. (8 units) in 14 hours. After that the patient took 5 units three times a day without untoward manifestations until about a month later when allergic symptoms recurred and indicated redevelopment of sensitivity. No further treatment was attempted.

Although the results of the tests indicate that the patient was hypersensitive to insulin itself, it is difficult to believe, as pointed out also by Allan and Scherer,¹⁰ that he could become hypersensitive to a material which is produced in his own

TABLE 1 Rapid Method of Desensitization in a Non Diabetic Case of Hypersensitivity to Insulin

DATE AND TIME OF INJECTION	AMOUNT OF INJECTION cc	UNITS	REACTION
INTRACUTANEOUS			
10:30 a.m.	0.01	0.4	Wheal 23 by 33 mm. with long periorbital, erythema 65 by 80 mm. marked itching
12:00 p.m.	0.01	0.4	Small wheal, erythema 25 mm.
1:40 p.m.	0.03	1.2	Small wheal, erythema 15 mm.
2:50 p.m.	0.01	1.2	None
3:40 p.m.	0.04	1.6	Slight erythema
6:15 p.m.	0.05	2.0	None
INTRAVENOUS			
8:15 p.m.	0.02	0.8	None
9:50 p.m.	0.04	1.6	None
9:55 p.m.	0.06	2.4	None
10:00 p.m.	0.08	3.2	None
10:30 p.m.	0.11	4.8	None
11:00 p.m.	0.16	6.4	None
12:00 p.m.	0.20	8.0	None

body." The possibility of species-specific molecular differences between animal and human insulins may be an explanation, although crystalline insulins derived from different sources appear to be identical. Since the exact composition of crystalline insulin is not known, however, it is possible that commercial crystalline insulin contains something else besides the hormone itself. This possible explanation receives support from the studies of Hansen and Eyer,¹² who found that twice crystallized insulin gave much weaker reactions than did crude crystalline insulin. Furthermore, in our case and in cases reported by Baker,¹³ Allan and Scherer,¹⁰ and Campbell Gardiner and Scott² the reactions from crystalline insulin were less severe than those following injections of standard insulin, and in a case mentioned by Joslin¹⁴ the patient was "extraordinarily sensitive to the four regular American preparations of insulin" but not to a crystalline form. If insulin itself were at fault one should expect the reactions to be equally intense, although in our case a possible desensitizing effect of preceding injections of standard insulin may explain the lesser reactions that followed the subsequent injections of the crystalline insulin. In the cases reported by Tuft³ and Davidson⁵ the reactions from crystalline insulin were just as pronounced as with other forms, and in Murphy Beardwood and Miller's⁶ first case they were even greater.

Abel, quoted by Davidson,⁵ rejected the theory that reactions to crystalline insulin are due to contaminants rather than to the hormone itself. He insisted that there is no ground for the statement that insulin is not a pure hormone but a mixture of substances, and he offered as the most plausible theory the conception that the different insulins, although having the same composition and crystalline form, differ in respect to the internal arrangement of their component amino-acids.

The relation of diabetes to allergic diseases in general is an interesting one. In our experience asthma or hay fever has rarely been observed together with diabetes in the same patient. Joslin¹⁵ also comments on the rarity with which it [asthma] is encountered in diabetes." Kern¹⁶ has shown that diabetes and allergy have a high reciprocal familial incidence but that they seldom occur in the same patient at the same time. Joslin¹⁴ cited a case in which asthma disappeared with onset of diabetes, and in the cases reported by Kraupl¹⁷ and Nonn¹⁸ improvement of diabetes followed attacks of allergic reactions to insulin. Kraupl thought it possible that the diabetic individual is not predisposed to allergic reactions.

It may be of significance in this connection to note that our patient (the only one with such severe general manifestations of sensitivity to insulin we have seen) and one reported by Sammis¹ did not have diabetes. Although definite conclusions cannot be drawn from this, it may mean that the incidence of allergic reactions to insulin is greater in the relatively small number of nondiabetic persons treated with insulin than it is in insulin-treated patients with diabetes.

The results in our case demonstrate that rapid desensitization is feasible and effective. It is superior to the slower methods used by Herold,⁷ Hansen and Eyer,¹² Bryce,¹⁹ and Collens, Lerner and Fialka,²⁰ not merely because it is less time consuming but especially because it may be a life saving measure when immediate and intensive treatment with insulin becomes imperative in such emergencies as coma or postoperative acidosis in hypersensitive patients with diabetes.

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REPORT ON MEDICAL PROGRESS

THE DIAGNOSIS OF THE VARIOUS ARTHRITIDES*

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MANY of the etiologic, diagnostic and therapeutic problems pertaining to the various arthritides are old medical controversies. They are excellent examples of the unknowns of medicine that confront the busy practitioner and the supposedly learned specialist. Although advances in the field of rheumatic diseases have been less numerous and less dramatic than in some of the other branches of clinical medicine, substantial contributions have been made in recent years. They are due largely to increasing interest and to the recently added facilities available for workers studying and caring for these socially and economically important diseases.

GENERAL INCIDENCE, SOCIAL AND ECONOMIC IMPORTANCE

Among the chronic diseases in the United States, "rheumatism ranks first in prevalence, second in producing chronic disability, second in invalidity (permanent disability) and fourteenth in causing death."¹ Similar data have been compiled for the Commonwealth of Massachusetts by Bigelow and Lombard.² These workers estimated that there were 140,000 individuals in this state suffering from rheumatism, 80,000 with heart disease, 56,000 with arteriosclerosis, 31,000 with Bright's disease, 25,000 with active tuberculosis and 10,000 with cancer. Nearly 85 per cent of the 140,000 individuals were over forty years of age. Complete physical disability was present in 4.2 per cent, or approximately 6,000 of the cases. Thirty per cent or approximately 42,000 individuals were partially disabled. The so-

cial and economic problems resulting from these diseases are manifold. The days of work lost and the resulting loss of income are most impressive even in this social and economic age, where figures mentioned usually run to seven digits.

CLASSIFICATION OF JOINT DISEASES

Classification of diseases of joints is essential to the diagnosis of the various arthritides. Many classifications have been proposed but no one of them has been universally adopted. The reason for this state of affairs is obvious. Our present inadequate knowledge of some of the arthritides does not permit the employment of the more detailed and all too cumbersome classifications.³⁻⁵ The more simple classifications unfortunately are based on erroneous and unproved assumptions and therefore are of little practical use.^{6,7} Considering the existing limitations of our knowledge of joint diseases, a classification based on etiology is preferable to one based on morbid anatomy. An etiologic classification is much more useful to the practicing physician in that the therapy indicated is more readily apparent once the diagnosis is made. Such a classification is readily made more complete and more useful as our etiologic knowledge of the arthritides advances. Preferring this type of classification, we use the one originally proposed by Allison and Ghormley,⁸ with slight modifications.⁹ Although not so complete as some might desire, its simplicity should appeal to the busy practicing physician.

I Joint diseases of known etiology

- I Traumatic, that is, associated with and the result of acute trauma, such as sprains, strains, internal derangements, fractures into the joint, traumatic synovitis and so forth

This is Publication No. 36 of the Robert W. Lovett Memorial for the Study of Crippling Disease, Harvard Medical School.

From the Medical Clinic, Massachusetts General Hospital and the Department of Medicine, Harvard Medical School, Boston, and the Massachusetts Department of Public Health.

The arthritic studies in this clinic are made possible in a large part by a grant from The Commonwealth Fund, New York City.

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2. Infectious that is, due to the tubercle bacillus, gonococcus streptococcus staphylococcus meningococcus and other organisms.
3. Neuropathic that is associated with tabes syringomyelia nerve injuries and leprosy
4. Metabolic that is, associated with gout.
5. Constitutional that is, associated with hemophilia.
6. Anaphylactic that is, associated with serum sickness.

II Joint diseases of unknown etiology

- 1 Degenerative joint disease (degenerative, hypertrophic or osteoarthritic)
 - a Primary; that is, the type so frequently encountered after the fourth decade of life. The joint disease resulting from the daily minor traumas of increasing age is pathologically indistinguishable from primary degenerative joint disease and is therefore classified as such
 - b Secondary that is the degenerative joint changes which ensue in consequence of intra-articular damage resulting from a previous acute arthritis, such as any of the acute specific infectious arthritides or acute recurring gouty arthritis or that due to repeated trauma
- 2 Rheumatoid arthritis (proliferative, atrophic or chronic infectious arthritis)
 - a Typical.
 - b Atypical (often called "nonspecific infectious arthritis" or "focal infectious arthritis")
 - c Spondylitis (Strümpell Marie type spondylitis rhizomelica spondylitis deformans spondylitis ankylopoietica, spondylitis osseans ligamentosa or rheumatoid arthritis of the spine)
- 3 Rheumatic fever

III Diseases of other skeletal structures of unknown etiology

- 1 Tenosynovitis.
- 2 Bursitis.
- 3 Dupuytren's contractures.
- 4 Myositis.
- 5 Fibrositis.

The above classification is probably self explanatory save for the divisions made under rheumatoid arthritis. Cases classified as typical rheumatoid arthritis seem to require no further comment. However the cases included under atypical rheumatoid arthritis do. This group includes cases that do not exhibit the characteristic history, habits and physical conditions observed in the typical cases of rheumatoid arthritis. The onset is usually sudden without preceding prodromal symptoms often following an acute infection or occurring in an individual with some obvious focus of infection. Such patients rarely complain of paresthesias, neurologic symptoms or increased vasomotor activity. The joint involvement is asymmetrical

and large joints are more commonly affected. The arthritis is frequently polyarticular and migratory. The monoarticular form is encountered. Such patients may recover completely even though the supposed causative focus of infection is not removed. These remissions or periods of complete recovery may last months or years but are almost always followed by a relapse. This type of rheumatoid arthritis may be characterized by a number of remissions and relapses before going into the chronic progressive phase.

The fact that the remissions frequently occur spontaneously has caused many workers to draw erroneous conclusions concerning the specific cause and cure of this the atypical form of rheumatoid arthritis. Such cases are not infrequently labeled the focal infectious type of arthritis or nonspecific infectious arthritis (because the causative agent has never been isolated). If in such cases one will allow for the passage of time before making an absolute diagnosis, the true nature of the type of arthritis present will usually be come all too apparent.

DIAGNOSIS

Much that one reads pertaining to the various arthritides is confusing and contradictory. As previously stated, there exists no uniformly adopted nomenclature. The etiology of the chronic arthritides remains undetermined. Most of the recently advocated forms of therapy prove to have little merit when their administration is rigidly controlled.¹⁰⁻¹³ This disconcerting state of affairs and the unrelentingly progressive course of the malignant type of rheumatoid arthritis constitute some of the reasons why many busy practitioners approach each new arthritic patient with a feeling of despair and complete absence of enthusiasm. Such an outlook is not very inspiring to the prospective patient and is not conducive to good therapy. This abject attitude is not fully justified. Our knowledge of the various arthritides is not so chaotic as it may appear. This is particularly true of diagnosis.

The diagnosis of disease of joints is in most cases relatively easy. As with other diseases, a correct diagnosis is based primarily upon a detailed medical history and complete physical examination. All too frequently the busy physician accepts the patient's diagnosis of rheumatism or arthritis and proceeds with the more commonly employed diagnostic and therapeutic procedures. Such a method of attack may be costly and may greatly inconvenience the patient especially so when a thorough eradication of all questionable foci is undertaken. Exhaustive diagnostic and therapeutic programs are often instituted when a detailed history and physical examination with or without a few well-chosen laboratory tests would have given the correct diag-

nosis and made it clear that the therapy indicated was a simple, straightforward procedure known for decades. It is not good medical practice to resort to surgical removal of the various suspected foci of infection when full doses of colchicine would completely relieve the gouty arthritis within forty-eight or seventy-two hours. This also applies to many cases of gonorrheal arthritis, degenerative joint disease and various other arthritides. Experience has taught us that as complete a knowledge as possible of the well-established clinical facts pertaining to joint disease is of much greater diagnostic and than all the more recently developed tests¹⁴⁻¹⁷. Thus it would appear wisest to devote the rest of this paper to a discussion of the diagnosis of joint diseases, even at the risk of being accused of being too elementary. Such a mistake seems justified when one appreciates that many ill-founded etiologic and therapeutic theories are due in part to incorrect diagnosis and an inadequate knowledge of the life course of the various arthritides.

No one of the laboratory tests employed is absolutely diagnostic. Finding an elevated fasting serum uric acid in a patient suffering from acute arthritis probably indicates the existence of gouty arthritis. However, one must remember that other diseases cause similar elevations of the blood uric acid and that the gouty patient may suffer from some other type of arthritis. Most other blood chemical tests are usually of little aid. The corrected sedimentation rate indicates the activity of the arthritis and not the type of arthritis present. It may be elevated in the non-infectious types. Serological tests such as the Wassermann, the gonococcal complement-fixation and undulant fever agglutination tests are of help only when considered in conjunction with the clinical facts. The various hemolytic streptococcus immunological tests (agglutinins, antistreptolysin, precipitins and so forth) are not diagnostic tests. Roentgenograms may be extremely helpful, particularly when correlated with the clinical findings, but here, too, there are many exceptions. Roentgenograms taken early in cases of acute infectious arthritis are usually negative and never diagnostic. A few weeks later they may be more helpful. The alterations detected by roentgenograms in the chronic arthritides may at times simulate each other. All too frequently the roentgenologist's interpretation is accepted as the final word, despite the history and the other findings. Considerable diagnostic help is obtained from cytological, bacteriological and chemical examinations of aspirated synovial fluid. Such findings should never be relied upon solely.

In order to cover concisely and yet as completely as possible the diagnosis of the various joint dis-

eases, they will be taken up in the order presented in the classification previously given.

Traumatic Arthritis

As previously mentioned, only acute trauma is included under the term "traumatic arthritis." This type of joint disease as a rule is not difficult to diagnose. The history and physical findings usually suffice. One must be aware, however, that trauma to a joint may mark the onset of acute arthritis due to a specific organism. It may precipitate an attack of acute gouty arthritis, or it may be the factor responsible for the localization of rheumatoid arthritis. In those cases where the clinical findings lead one to suspect some such complicating factor, aspiration of the joint is most helpful. If the total cell count and percentage of polymorphonuclear leukocytes are not increased, the suspected complications can be dismissed.

Infectious Arthritis

Such arthritides are the direct result of invasion of the articular structures by a specific organism. These organisms reach the joints via the blood stream, therefore, with the exception of tuberculosis, in a large percentage of cases invasion of the blood stream will be accompanied by a chill, chilly sensations and a rise in temperature. There may or may not be the accompanying findings which characterize a bacteremia or a septicemia. The onset of the arthritis is acute. It is frequently polyarticular and migratory the first few days, finally settling in one or more joints, usually large ones, although no joint is exempt. The joint involvement is rarely symmetrical. This type of onset is seldom encountered in any other type of acute arthritis. Suspicion having been directed to a diagnosis of acute infectious arthritis, one must next determine the type if possible. Gonorrheal arthritis is first suspected as it is commoner than the others, particularly in the adult. A reliable history helps. The demonstration of the organisms in aspirated joint fluid allows for a diagnosis of proved gonorrheal arthritis. Recovery of gonococci from a genitourinary focus suggests gonorrheal arthritis. Cultural methods are superior to relying on demonstration of the organisms by smear. The gonococcal complement-fixation test is very helpful, but not absolutely diagnostic. The existence of the other types of specific infectious arthritis may be suggested by the history. Bacteriological tests should be relied upon whenever possible. This type of arthritis is frequently extremely painful. The cardinal signs of inflammation are usually present. Roentgenograms rarely show changes until the third week of the disease. If organisms are present, the syno-

vial fluid may become purulent. If not arrested this type of arthritis causes destruction and crippling. With the advent of sulfanilamide and other allied compounds, such end results should be encountered less frequently in the future provided the diagnosis is made early and the treatment administered properly.¹¹⁻¹⁶

The articular lesions of congenital and acquired syphilis should not be overlooked. They belong in the specific infectious arthritis group. The articular manifestations of congenital syphilis are known as Clutton's joints or tenosynovitis syphilitica. Being painless they are frequently overlooked. They are commonly misdiagnosed as tuberculous arthritis, particularly so when monoarticular in type. Symmetrical painless effusions in a child should always lead one to suspect Clutton's joints. Although usually symmetrical, the monoarticular form is seen. Such articular manifestations are rarely encountered in the adult. The knee joints are most frequently affected, but no joint is exempt. The only discomfort experienced by the patient is stiffness on extremes of flexion and extension because of the joint effusion. In the presence of such joint signs, one should look for the other stigmas of congenital syphilis. The recognition of this type of joint disease is most important because such lesions clear completely, even though specific therapy is not administered. The articular manifestations of secondary syphilis rarely offer diagnostic difficulties save when we fail to think of them.

The rarer types of specific infectious arthritis such as those encountered in chronic meningococcal septicemia, undulant fever, the various dysenteries, Haverhill fever, lymphopathia venereum subacute bacterial endocarditis, Reiter's disease, scarlet fever and the exanthemas should be considered in the patient presenting an unusual or atypical type of arthritis.

Gouty Arthritis

This type of arthritis is encountered as frequently as ever, despite statements to the contrary made during the last decade or two. Recent studies have shown that the incidence of gout in any community is directly related to the knowledge of the disease. As the latter increases, so does the incidence of gout.²¹ If one is to demand the presence of tophi, characteristic roentgenographic changes and hyperuricemia before making the diagnosis of gout, many cases of presumptive gouty arthritis will go for years undiagnosed or mislabeled. Increasing suspicion of its existence plus a better knowledge of the disease

has resulted in a marked increase in the number of cases so diagnosed each year in this clinic.

As in other types of joint disease, so too in gouty arthritis an accurate history is most important. It alone will enable one to suspect the correct diagnosis in the majority of the cases. Certainly a suspicious history should always call for a therapeutic trial with full doses of colchicine.²¹ This therapeutic test can be and always should be carried out even if uric acid determinations are not possible. A history of recurrent attacks of arthritis with absolutely complete freedom of joint symptoms between them should always lead one to suspect gouty arthritis. Gouty arthritis is rarely chronic from the onset. Polyarticular involvement occurs in about 5 per cent of cases. The younger the individual, the more likely the involvement is to be polyarticular of the simultaneous or migratory type. This type rarely involves the large toe, and the attacks are of weeks duration rather than the usual seven to ten days. The fever is more marked and may last weeks. This type is rarely afebrile. It signifies severe gout and crippling ensues at a much earlier age. It is frequently misdiagnosed as rheumatic fever.

Gout is an inherited disease, therefore a family history of gout is frequently obtained. The average age of onset has been recorded as forty years,²² although it may begin at a much earlier age.²¹ There may or may not be a history of a precipitating event. Such factors include physical trauma, physiologic trauma, gastronomic sprees and worry.^{1, 24} Operative procedures have been known to induce attacks. One authority⁴ states that gout should be suspected in all cases of acute postoperative arthritis, particularly in men. The common prodromal symptoms are nausea, indigestion, melancholia, polyuria, nocturnal stiffness, aching and so forth. More attacks occur between April and June than at any other time of the year. The interval between the first and second attacks is variable, it may be months or years, but the average is eighteen months. It usually becomes less with increasing age. The average duration of an attack is thirteen days. It may be as short as twenty four hours or last for weeks.

If one suspects gout, a diligent search for tophi should be made. They are most commonly found in the helix of the ear. They are white cream colored or yellow, varying in size from that of a pin head to that of a pea. Except in severe gout they rarely appear until some other symptoms of the disease have been present for ten years or more. They are pathognomonic of gout but should never be considered as such until monosodium urate crystals have been demonstrated or a positive murexid test

has been obtained. They are also found in the cartilages of the nose, along the tendons of the fingers, hands, toes and feet, the patellar tendons and in the bursas of the patella, olecranon and Achilles tendon. They should not be confused with the subcutaneous nodules of rheumatic fever and rheumatoid arthritis. When the overlying skin breaks down, a mixture of chalklike material is extruded.

Although gout commonly involves the great toe, it does so in only 50 per cent of cases in the initial attack. This is true whether the attack is monoarticular or polyarticular. The spine, sacroiliac joints, shoulders and hips are rarely involved. Joint effusions do occur.

The history, although very suggestive, is of limited diagnostic aid when dealing with a patient suffering from his first attack of gouty arthritis. In most cases the onset is characterized by the instantaneous appearance of severe pain. This may come at a time when the patient has considered himself well. It is most important for the physician to realize that, as stated above, gout affects the big toe in only half the cases in the initial attack. Furthermore, no joint is exempt. The rapid appearance of articular swelling is much more characteristic of acute gouty arthritis than is the sudden onset of pain. Swelling of the foot may be so marked within an hour of the onset of acute gouty arthritis involving the first metatarsophalangeal joint as to necessitate cutting off the shoe.

In gouty arthritis the swelling extends farther beyond the joint margins than is observed in any other type of arthritis. Acute gouty arthritis more nearly resembles septic inflammation or extensive cellulitis. There may be associated lymphangitis. The overlying skin is red, tense and shiny. The superficial veins may be markedly distended. The tenderness is exquisite, as it subsides, pitting edema is demonstrable. With disappearance of the joint swelling, desquamation of the cuticle and itching follow. The latter finding is almost diagnostic of gouty arthritis. The pain may be extremely severe, often described as crushing, worse during the night and letting up in the early morning. These physical findings coupled with the history of sudden onset are of great diagnostic value.

Gouty arthritis having been suspected, confirmation of the diagnosis is rarely difficult. The dramatic response to full doses of colchicine is rarely observed in other types of arthritis. Recourse to laboratory tests in the case of the patient with a gouty arthritis reveals a mild to moderate leukocytosis, an increase in mononuclear leukocytes, a normal or increased sedimentation rate and a hyperuricemia. An elevation of the serum uric acid is nearly always present in untreated presumptive

or tophaceous gout.²¹ The determination is of most value when done on a fasting blood sample.²²⁻²⁷ One can use either the Folin²⁸ or the Benedict²⁹ method. With either method one rarely obtains a serum uric acid value of less than 6 mg per cent in the gouty patient. Exceptions to this rule are rarely encountered in gouty patients.²⁵⁻²⁷ Determination of uric acid excretion is of no diagnostic aid. Evidences of mild renal impairment are frequently encountered in gouty patients.²⁻³⁰⁻³¹ Many of them die of uremia because of a complicating chronic nephritis.³¹ "Chronic arthritis associated with distinct renal impairment should always suggest gout until proved otherwise."²² The same might be said of the arthritic patient with a history of having passed gravel or renal calculi.

The roentgen-ray findings suggestive of gouty arthritis are punched-out areas, usually 5 mm or more in diameter, most commonly located in the subchondral bone of the base or head of the phalanges of the hands and feet. Such changes may be late in appearing. In Hench's²² series, 19 cases with tophi and hyperuricemia had had their disease twenty-eight years or longer and yet no roentgenographic changes were present. Marginal hypertrophy of the bones involved is a frequent finding. The punched-out areas should not be confused with those seen in hypertrophic and rheumatoid arthritis. In the latter, generalized decalcification is usually present. Occasionally similar findings are encountered in syphilis, leprosy, yaws, tuberculosis and sarcoid. Without the clinical history the roentgenologist should not be expected to make the diagnosis. The clinician should never accept the roentgenologist's diagnosis unless the clinical facts are in accord with the diagnosis of gouty arthritis.

More detailed information concerning the gouty patient can be obtained by consulting the more recent publications.²²⁻²⁴⁻²⁶⁻³² It is interesting that effective therapy is little different from that prescribed years ago, except that it would appear that rigid restriction of the purine intake is not justified or indicated. We never employ cinchophen or any of its compounds because of the risk of inducing acute yellow atrophy and the fact that the pill form of colchicine is equally if not more efficacious.

Neuroarthropathies

Neuroarthropathies are most commonly associated with tabes, syringomyelia, nerve injuries and leprosy, in the order mentioned. The onset being insidious and painless, the patient usually seeks medical aid because of joint enlargement. Occasionally the onset is sudden and painful. This

latter type progresses much more rapidly. Joint effusions are the rule, and may be hemorrhagic. Increased joint mobility is dependent on the size and duration of the effusion, the extent of the joint disorganization and the frequency with which it has been traumatized. In the advanced cases all types of deformities and dislocations are encountered. Flail joints are seen. An occasional patient complains of recurrent joint pain. The roentgenograms of the neuroarthropathies reveal destruction of the articular cartilage, an irregular joint line, bone resorption, bone formation, exostoses, loose body formation and at times calcification of the ligaments and regional muscles. In tabes the weight bearing joints and the spine are more commonly affected, whereas in syringomyelia the joints of the upper extremity are more frequently involved. Arthropathy may be the first sign of tabes. The other most constant presenting tabetic signs are Argyll Robertson pupils and absent knee jerks. The diagnosis of neuroarthropathy should always be considered when pain, tenderness and increased heat are absent. It is established by recognizing the disease of which it is a part.

Constitutional Arthritis

The one constitutional disease in which arthritis is frequently encountered is hemophilia. The articular manifestations may be the result of a single intra-articular hemorrhage or of repeated intra-articular hemorrhages. The acute type may occur at rest, although it usually follows some degree of traumatization. The joint symptoms of pain and swelling vary with the extent of the hemorrhage and the rapidity with which the intra-articular pressure rises. In some cases such symptoms may be marked. Local heat and redness are rarely present. The overlying skin may be discolored. There may be an associated fever and leukocytosis. In the acute stage roentgenograms reveal joint distention and peri-articular swelling without associated bone changes. The hemorrhagic effusion causes an irritative synovitis. The tissues tend to return to normal as the blood is absorbed. Following repeated hemorrhages the joints may fail to return to normal. In such cases the symptoms of stiffness, pain and swelling may persist for months. It may progress to a chronic arthritis with a resulting fibrous-tissue ankylosis. In the chronic arthritis of hemophilia, the roentgenograms reveal a characteristic irregular spotty type of articular cartilage destruction, subperiosteal and subchondral cavities and cysts, marginal exostoses and dense, thickened subsynovial tissues (due to the large amounts of iron contained therein). Such roentgenographic changes should not be

confused with those of degenerative joint disease or tuberculous or rheumatoid arthritis. The diagnosis depends on the history of a bleeding tendency and the onset of acute painful swelling of a joint following minor trauma occurring in a young man. When in doubt, aspiration of the joint with a small-gauge needle should be undertaken.

Anaphylactic Arthritis

The arthritis of serum sickness is the only type of arthritis which can be classified as anaphylactic or allergic in nature. The arthritis of serum sickness may appear one to twenty-one days following the administration of one of the therapeutic serums, even in small amounts (5 cc). The onset is abrupt, with associated fever, itching, urticaria, adenopathy, splenomegaly and at times abdominal symptoms. A leukocytosis precedes the onset, a leukopenia supervenes. Eosinophilia may be present. Evidence of renal irritation is at times demonstrable. The arthritis may be primarily a severe arthralgia with little evidence of objective signs. At other times redness, increased heat and swelling of the joints may be marked. The arthritis is often migratory, affecting chiefly the large joints. It usually disappears within two to seven days, but may last three or more weeks. It clears completely, leaving no residual signs. This type of arthritis should never offer any serious diagnostic difficulties.

Degenerative Joint Disease

This type of joint disease is commonly spoken of as hypertrophic or osteoarthritis. We^{32, 34} prefer the term degenerative joint disease because it describes more accurately the pathologic changes encountered and we discourage the use of the word "arthritis" when speaking of this disease because there is little or no evidence of inflammation. Experimental and pathological studies reveal that articular cartilage differs from most other body tissues in that it possesses a very limited ability to repair itself. It appears that this limitation is not a function of the age of articular cartilage, but is directly related to the fact that articular cartilage is a relatively avascular tissue in which the matrix greatly exceeds the cellular elements. Because of this limited ability of articular cartilage to repair itself the wear-and-tear changes of daily life become accumulative with increasing age, and in consequence intra-articular changes indistinguishable from hypertrophic arthritis are demonstrable in the knee joints of all individuals over fifty years of age. That the production of this type of joint disease may be explained solely on this basis is suggested

by the fact that similar changes ensue if a single joint is subjected to unusual use or to an intra-articular derangement such as patellar displacement³⁵ From clinical observations it is apparent that such changes can also be produced, or if present can be hastened, by increasing the load which the joint has to carry or by impairing its normal mechanics³⁴ If such factors have been operative since early childhood, the intra-articular changes will be demonstrable at a much earlier age In all probability the type of cartilage one inherits governs in part the early onset of such joint changes as well as the rapidity with which they progress

The primary type should be readily diagnosed It is much more frequently encountered than any other type of joint disease The history of an insidious onset occurring after the fourth decade of life and persisting for any period of time practically precludes the existence of most types of arthritis except those that are chronic in nature The absence of fever and other evidences of infection tends to rule out most of the chronic arthritides due to infectious agents In most cases the diagnosis rests between degenerative joint disease and rheumatoid arthritis

On the basis of symptomatology alone, one encounters a general and a local type The disease rarely occurs in the monoarticular form except in cases where a single joint has been subjected to long-continued use or trauma, such as occurs in certain industrial workers Many patients may complain of symptoms referable to one joint, yet roentgenological examination reveals the same or an even more severe grade of degenerative joint disease in the opposite joint In most cases close examination gives evidence of involvement of articular structures other than those complained of The joints most commonly involved are the terminal phalangeal joints, the knees, the lumbar spine, the first metatarsophalangeal joints, the sacroiliac joints, the lower portion of the cervical spine, the shoulders and the hips The mid-phalangeal joints of the fingers and the metacarpophalangeal joints of the thumbs are less commonly affected Although no joint is exempt, these patients rarely complain of symptoms referable to the elbows, wrists and ankles The involvement is rarely as widespread as in rheumatoid arthritis

The terminal phalangeal joint lesions are spoken of as Heberden's nodes Although they are pathognomonic of the disease they are not present in every patient They are commoner in women than in men The symptomatology referable to these joints and their appearance varies greatly from patient to patient In some they

are never a cause of complaint, some seek medical treatment because of their unsightly appearance, others because the joints are sensitive and ache Some patients desire medical treatment because they fear that such joint signs represent the first objective evidence of a beginning crippling arthritis In those patients experiencing symptoms with the development of Heberden's nodes, the complaints are aching, tenderness on pressure, slight stiffness, numbness and tingling Except for the occasional case there is little to demonstrate at the time of onset other than slight joint swelling In the exceptional case, early in the disease, the terminal phalangeal joint may be red and bulbous, fluctuant and tender on pressure Such signs usually subside in eight to twelve weeks, leaving the tell-tale evidence of the typical Heberden's node Involvement of all fingers may be present from the onset More commonly the joints of the index and fifth fingers are the first to be affected Such joints may ultimately assume a gnarled, knotted appearance They never become truly ankylosed Rarely a small cyst surmounts the nodosities

Patients with degenerative joint disease rarely complain of symptoms other than those referable to the joints When they do, they are usually due to disease of some other system Therefore, the prodromal and constitutional symptoms so frequently seen in rheumatoid arthritis such as weakness, easy fatigability, anorexia weight loss, fever, tachycardia, vasomotor symptoms, paresthesia and muscular weakness are not encountered The onset is insidious In many patients, particularly the obese, the first complaints are pain and stiffness in the knees and back In fact, the obese patient may develop symptoms at a much earlier age than does one of normal weight The pain is invariably relieved with bed rest Some patients complain of grating and creaking in one or more joints, with or without associated stiffness, aching or pain The pain may be accentuated by many factors, particularly by exercise and by changes in the weather Generalized stiffness is a common complaint It is present on awakening or after sitting for a time, only to disappear after the patient has limbered up or walked a short distance The most distressing symptoms are encountered in patients with marked deformities of the knees (*genu valgum* or *genu varum* deformities) and *malum coxae senilis* The latter affliction is the most disabling and painful manifestation of degenerative joint disease Any of the above-mentioned symptoms may fluctuate considerably Some patients may experience complete relief for varying periods of time The reasons for such fluctuations are

not always apparent. In some cases they are directly related to living in a warm climate. In other patients, although the symptoms are never severe, they continue to persist. In such cases they may be looked on as a nuisance rather than as a disability.

Patients with degenerative joint disease are as a rule well nourished or obese. They do not exhibit evidence of pallor, weight loss, atrophy of the skin and muscles, generalized adenopathy, increased vasomotor activity, pigmentation and subcutaneous nodules so frequently seen in patients with rheumatoid arthritis. The examination of the joints is negative except for restriction of motion demonstrable in *malum coxae senilis* and marginal proliferation of the terminal phalangeal joints, the knees, the first metatarsophalangeal joints and occasionally the midphalangeal joints.

These patients rarely have anemia or leukocytosis, and these conditions when present should be ascribed to some other cause. The sedimentation rate in occasional cases is elevated for some reason as yet unknown. The non-filament counts are normal. Agglutination tests against streptococci are negative. The uric acid is normal. Lowered basal metabolic rates are encountered no more frequently in this group than in other individuals of corresponding age. The fasting serum calcium, phosphorus and phosphatase determinations are normal.

A roentgenogram may be negative or show only slight changes, yet when the joint in question is opened, examination may reveal marked changes characteristic of so-called hypertrophic arthritis. Nevertheless the roentgenographic appearance of degenerative joint disease is quite distinctive from rheumatoid arthritis. Decalcification except as a manifestation of age is not present. The first changes noted are narrowing of the joint space, with sharpening of the articular margins. Subsequently, marginal proliferation and condensation of the subchondral bone ensue. Small cysts are sometimes observed near the articulating surface. Bone destruction and irregularity of the joint line are observed only in well advanced Heberden's nodes. Soft tissue changes are rarely demonstrable. One should never let the diagnosis rest solely with the roentgenologist. The roentgenographic findings should be looked on as one piece of evidence to be considered along with the history, physical examination and other laboratory tests in arriving at a final diagnosis. One must always remember that advanced changes of degenerative joint disease will ensue rapidly in a joint previously affected by a gouty, specific infectious or rheuma-

toid type of arthritis as well as repeated trauma. This we term secondary degenerative joint disease.

Rheumatoid Arthritis

The classic case of typical rheumatoid arthritis is readily recognized. The disease respects neither age, sex, race nor social position, although it affects women more often than men, white people more often than Negroes and the poor more often than the rich. In addition to the articular involvement, which is usually symmetrical and more likely to affect small joints first, the patients complain of constitutional, vasomotor and neurologic symptoms. These associated symptoms precede those referable to the skeletal system, and in many cases persist throughout the course of the disease. Such symptoms include weakness, easy fatigability, anorexia, weight loss, increased vasomotor activity, symptoms of Raynaud's disease and numbness, tingling, burning and stinging of the fingers and toes. Localized muscle weakness may be marked, with or without associated muscle twitchings and tremors. The symptoms referable to the skeletal system are muscle stiffness, aching and pain, neuritic like pain, generalized stiffness, and joint stiffness, aching, pain and swelling. Itis and scleromalacia perforans are occasionally seen. The disease may be unrelentingly progressive from the onset but is more commonly characterized by remissions and relapses of varying degree and duration. In a small percentage of cases the remissions are complete and of years duration; in the majority they are incomplete and short-lived, with recurrent symptoms and persisting, tell-tale evidence of previous fascial and joint involvement. Irrespective of the initial course of the disease, increasing evidence of progression occurs with the passing of time, leading in many cases to partial or complete incapacitation.

On physical examination such patients often show a characteristic pallor, evidence of weight loss, obvious symmetrical joint involvement of varying degrees, skin and muscle atrophy and usually generalized lymphadenopathy. Splenomegaly is encountered. Pigmentation when present is quite characteristic, consisting of a peculiar bronzing of the skin which is most marked over the face and extremities. Psoriasis occurs in 3 per cent of cases. Such cases are often termed psoriatic arthritis. To date there is little justification for considering these patients as suffering from a distinct disease entity. The subcutaneous nodules of rheumatoid arthritis probably constitute the most characteristic lesion of rheumatoid arthritis. They are present in about 20 per cent of cases.

They are most commonly found over the extensor surfaces, particularly of the elbow. When noted in this region they are situated 3 to 5 cm distal to the elbow joint. They are also found along the tendons of the fingers and toes, in the olecranon bursitis and over the patellas, scapulas, spinous processes, sacrum and scalp. They vary in size from scarcely palpable, seed-like particles to lesions several centimeters in diameter. They are frequently attached to underlying structures but the overlying skin is freely movable. They rarely cause pain. They usually persist for months and often for years. When in doubt the differentiation of rheumatoid nodules can usually be made by microscopic examination.

A low-grade fever is not uncommon. In the more fulminating cases, particularly in children (Still's disease), a spiking temperature of 103 to 105°F may be maintained for weeks. A moderate tachycardia, usually persistent, is the rule even in those cases where fever is not a marked feature of the disease. A moderate anemia is frequently observed. More extreme grades of anemia may develop. There is usually no leukocytosis, or if present it is slight. In the cases characterized by a marked febrile response, a leukocytosis of 10,000 to 20,000 is frequently encountered. In children during the febrile period it may go as high as 40,000 or 50,000. In chronic cases a leukopenia may be present. There is usually an increase in the proportion of non-filamented cells. The sedimentation rate is almost always increased in rheumatoid arthritis, the increase usually being directly proportional to the severity of the disease. The streptococcal agglutination and precipitin tests are not of sufficient diagnostic aid to justify their being done routinely.

Early cases show no roentgenographic changes. Later the more typical manifestations are readily demonstrated. The most characteristic of these is generalized decalcification. Joint effusions are a prominent feature of this disease. Early periarticular soft-tissue swelling is the rule, it regresses if the disease persists. As progression occurs, narrowing of the joint spaces, cartilage destruction and cortical erosion are seen. Later fibrous or bony ankylosis may ensue. Subluxation and dislocation of the phalanges are common findings in long-standing cases.

The differences between the typical and atypical types of rheumatoid arthritis have been previously discussed.

Rheumatoid spondylitis is classified as a form of rheumatoid arthritis because peripheral joints are often involved preceding or following the first symptoms referable to the spine. The most striking difference between the generalized and

spinal types is the sex incidence. In the latter the ratio of men to women may be as high as 20:1, whereas in the former the ratio is 2:1 or 3:1 in favor of women. In uncomplicated cases of spondylitis the articulations involved are the small joints of the vertebrae, the sacroiliac joints, the hips and the shoulders. By means of roentgenological examination it is found that the majority of cases show their first change in the sacroiliac joints. This is not surprising knowing that sciatica is one of the commonest symptoms in most cases of rheumatoid spondylitis. The onset of this disease may be sudden or insidious, more commonly the latter. Besides sciatica the patients complain of pain and stiffness of the spine and pain on deep breathing, coughing or sneezing. Girdle pains and pains down the extremities are encountered. Some degree of rigidity of the spine is almost always present. Exquisite tenderness over the spinous processes may be elicited. Spasm of the spinal muscles is a frequent finding. The chest expansion and vital capacity are reduced. Constitutional symptoms of varying degree are usually present. Fever and leukocytosis of the same grade seen in the typical cases of rheumatoid arthritis are observed. The sedimentation rate is invariably increased. As the disease progresses, pain may be less, but motions of the spine are more limited. The process may remain localized but usually spreads so as to involve the entire spine. Involvement of the shoulders and hips occurs frequently. In those cases where all mobility is lost the spine assumes the characteristic "poker-back" appearance. The roentgenograms of rheumatoid arthritis of the spine are quite different from those of degenerative joint disease of the spine. Early cases may show no changes or only slight alterations in the sacroiliac joints. In the more advanced cases there is present generalized osteoporosis, involvement of the small intervertebral articulations and calcification of the anterior and lateral ligaments of the spine in addition to fusion of the sacroiliac joints.

Rheumatic Fever

Rheumatic fever is usually readily diagnosed. Occasionally it may simulate rheumatoid arthritis. In such cases only the passage of time and subsequent developments will enable one to make the correct diagnosis. Rarely, an early case of acute specific infectious or polyarticular gouty arthritis may be difficult to differentiate from rheumatic fever.

Other Skeletal Diseases

Most of the previously mentioned skeletal diseases of unknown etiology are readily diagnosed.

Space does not permit their being discussed. The articular lesions of acute disseminated lupus erythematosus, periarteritis nodosa and other rare diseases are frequently mislabeled.

Endocrine Arthritis

Although the term endocrine arthritis is frequently used, no one has presented sufficient evidence to prove that such a disease entity or disease entities exist. It is our belief that the term "menopausal arthritis" means little more than the occurrence of degenerative joint disease or rheumatoid arthritis just prior to, during or following the menopause. The thyroid gland and other glands of internal secretion have been incriminated from time to time, but without sufficient data to prove that endocrine dysfunction plays a major role in the production of any one of the arthritisides. During the menopause, many women will complain of various "algias." The exact significance of these is unknown. In many cases they may represent little more than the aches and pains encountered by most individuals from time to time, but during the sensitive state of the menopause they are accentuated. In some patients, such complaints are relieved when appropriate substitution therapy is administered.

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Space forbids discussion of many of the other interesting problems pertaining to diseases of joints. These will be found in some of the more recent publications.^{2, 22, 27} The physician interested in a detailed review of the current English and American literature pertaining to the problems of rheumatism and arthritis should consult the reviews published each year in the *Annals of Internal Medicine*.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25401

PRESENTATION OF CASE

A sixty-one-year-old American housewife was admitted complaining of pruritus and jaundice.

About three months before admission she noted the onset of generalized itching and burning of the skin. One week later jaundice appeared and gradually deepened up to the time of entry. After the development of jaundice she had consistently noticed clay-colored stools and very dark urine. With the pruritus a papular eruption developed over the legs and trunk, it was not pustular and not due to scratching. Since the appearance of the jaundice she had also been aware of a non-tender mass protruding in the epigastrium on standing. For two months she was occasionally nauseated but did not vomit. Her appetite failed but she had marked craving for fluids, especially fruit juices. She avoided fatty foods because they caused nausea. During the past month she had tired easily and occasionally experienced palpitation. She noticed dyspnea on exertion and had ankle edema, appearing in the late afternoon and subsiding during the night. There had been no orthopnea or pain. She had lost 20 pounds in weight after the onset of her illness. There was no past history suggestive of gall-bladder disease, and she had not had gastrointestinal complaints in previous years.

Physical examination showed a well-developed and nourished, jaundiced woman weighing 180 pounds. Examination of the heart was essentially negative. The blood pressure was 130 systolic, 64 diastolic. The lungs showed persistent fine rales at both bases, extending to the angles of the scapulae. The liver edge was palpated 3 cm. below the costal margin. A notch was palpated toward the midepigastrium, and there was a hard mass attached to the liver edge at this point. There was only slight abdominal tenderness, and no spasm. No signs of fluid could be elicited.

The temperature was 98.6°F., the pulse 70, and the respirations 18.

Examination of the urine showed the presence of bile, and the sediment contained 10 to 15 white cells per high power field. The blood showed a red-cell count of 4,080,000, and a white-cell count of 10,000 with 77 per cent polymorphonuclears. The

serum nonprotein nitrogen was 20 mg. per 100 cc., the chlorides 102 milliequiv., the carbon-dioxide combining power 56.4 vol. per cent, the protein 5.9 gm. per 100 cc., the van den Bergh, biphasic, 13 mg. bilirubin per 100 cc. and the cholesterol 379 mg. per 100 cc. A blood Hinton test was negative.

Barium enema x-ray studies were negative. A gastrointestinal series showed no esophageal varices. The stomach was long and pushed somewhat laterally by a large liver. There were no other abnormalities. Two plain films of the abdomen showed no evidence of opaque stones in the gall-bladder region. X-ray films of the chest showed a slightly high diaphragm. The lung fields were normal. The left ventricle was slightly prominent, although the heart was not enlarged. The aorta was tortuous, the aortic knob calcified.

On the third hospital day examination of the abdomen showed the right lobe of the liver to be non-tender and not smooth. There was a hard nodular mass, possibly more than one, at the liver edge in the right midclavicular line. The spleen was not palpable. No lymphadenopathy or breast nodules were noted. On the fifth hospital day a peritoneoscopy was done. The edge of the liver was smooth and sharp, and the liver was greenish-brown. Both lobes were seen and showed no evidence of either metastatic cancer or cirrhosis. In the region of the gall bladder there was a mass 6 or 7 cm. in diameter which was pearl-gray and very firm in consistence. There was no evidence of metastatic disease in the peritoneal cavity. On the twelfth hospital day it was noted that the blood prothrombin level had risen from 75 to 95 per cent under vitamin K and cholic acid therapy. On the eighteenth hospital day a laparotomy was done.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM B. BREED. In brief this case is that of a sixty-one-year-old woman with painless jaundice of three months' duration without any gastrointestinal symptoms except anorexia and distaste for food, which are explained by the presence of jaundice. The dyspnea on exertion and edema are not very significant at the moment unless we find something farther along to indicate that she did have heart disease, the story sounds as if they were secondary to anemia or malnutrition.

Just considering the history and physical examination, one has to determine first of all whether the jaundice was due to intrinsic liver disease or to obstruction of the common duct. If it was obstruction, was it due to gallstones or to cancer of the pancreas, of the ampulla or of the bile ducts of the gall bladder itself with pres-

sure on or invasion of the common duct? The fact that it was painless does not necessarily rule out a stone in the common duct, but it does suggest that such was not the case. Also, the presence of a mass in the region of the gall bladder brings up the question of Courvoisier's law, which as I remember it, is as follows: "If the obstruction is due to a gallstone in the common duct, the gall bladder is not palpable, if it is due to cancer the gall bladder is enlarged and often palpable." Assuming, then, that the mass in the right upper quadrant was the gall bladder, that leads us away from the common duct and toward some malignant neoplasm, either cancer of the ampulla, the pancreas or the gall bladder itself or more remotely, a primary cancer of the liver with obstruction by invasion.

The blood showed a moderate anemia. I presume the Graham test was not done because it is of no value in the presence of marked jaundice.

On the third hospital day examination of the abdomen showed the right lobe of the liver to be non-tender and not smooth. That is an ambiguous statement. I do not know what they mean by not smooth. Was it really nodular? The examiner was apparently in doubt, and it also leaves me confused. "There was a hard nodular mass, possibly more than one." On direct examination one has to make up one's mind.

Following peritoneoscopy, it is stated: "The liver was greenish brown." Is that normal? Dr. Mallory?

DR. TRACY B. MALLORY: A greenish-brown color indicates jaundice and also suggests that the jaundice is obstructive rather than intrahepatic. In all probability the color would be orange yellow if the disease were intrahepatic.

DR. BREED: The reason I did not bring in the question of metastatic cancer of the liver is that I had already read the report following peritoneoscopy to the effect that there was no evidence of metastases in the liver. That is not conclusive of course, because mistakes are sometimes made by peritoneoscopy, but it is a fairly definite statement.

DR. MALLORY: Metastases may be within the substance of the liver and not present on the surface, so that even on abdominal exploration they can be missed, but it is unusual.

DR. BREED: So we cannot rule out a metastatic process, there is no evidence to point to it but some to point away from it. That is the best one can say.

In the region of the gall bladder there was a mass 6 or 7 cm. in diameter which was pearl gray and very firm in consistence. I have to ask another question. Could this appearance

be a dilated gall bladder? Could the examiner be sure, with this instrument?

DR. MALLORY: He could push the end of the instrument against the gall bladder and get a sensation of whether it was firm or not. With experience one is able to make very reliable observations in such a manner, as the experienced gynecologist comes eventually to feel with his curet.

DR. BREED: I take it that 100 per cent prothrombin is normal. They found it to be 75 per cent and gave vitamin K with bile salts and raised it to approximately normal before operation. They then operated on her and found out what this was.

I do not know how we can locate the lesion. I think she had cancer. She might have had a primary cancer of the liver, although I believe cancer of the liver is ordinarily internal and does not present on the surface.

DR. MALLORY: I should question that statement, Dr. Breed.

DR. BREED: Of course if it were a primary tumor of the liver, it was not widespread enough to cause hepatic insufficiency, however it did cause jaundice. There is a mechanical element here somewhere, I am certain. As to just what was causing obstruction to the common duct, I am in the same predicament that the surgeon was when he operated—and I do not believe any one could tell. The only thing one can do is to take a side and to assume it was due either to obstruction or to intrinsic liver disease. I shall take the obstructive side and, furthermore, say that the obstruction was due to cancer rather than to a gallstone. As to its primary site, I have no idea. I should say it probably was not caused by metastatic disease from cancer in the sigmoid or something of that sort.

A PHYSICIAN: How about the stools?

DR. BREED: They were clay-colored and not bloody.

A PHYSICIAN: The stomach was pushed somewhat laterally by the large liver. Does that mean anything?

DR. BREED: This may have been due to the mass that we are talking about rather than to the liver itself. I am not sure that the x-ray men could say that the shift was caused by the liver. It may even have been due to a mass in the liver itself.

A PHYSICIAN: The history says that she had a marked craving for fluids. The urine examination says nothing about sugar.

DR. BREED: I should agree with you that that is worth looking into for a question of involvement of the pancreas.

DR MALLORY While in the hospital there were several reports on the stools—one was gray-brown, three yellow and four white

A PHYSICIAN It could not have been barium?

DR MALLORY The fifth stool was said to have had barium in it. Nine urines were negative for sugar, three showed a green test

DR BREED That means nothing. Was the blood sugar determined?

DR MALLORY No. All urines contained from + to ++++ bile

DR BREED Is primary cancer of the liver always a hepatoma?

DR MALLORY No, there are two kinds. You can have a hepatoma, a tumor of liver cells, or a primary carcinoma of the intrahepatic bile ducts, which is histologically just ordinary adenocarcinoma. I shall add one other point in this geographic area: primary hepatoma never occurs in a patient who does not have cirrhosis of the liver. That is not true in China, where it occurs in people who are infected with flukes, or in Java, where it is the commonest kind of cancer, without any reason that we know of. Intrahepatic bile duct cancer can occur without cirrhosis.

DR BREED If she had brown stools and a serum bilirubin no higher than 13 mg per 100 cc, this suggests that there might not have been complete obstruction, and the more you think about it perhaps the more the question of primary carcinoma of the bile ducts comes to the fore as the best bet, so to speak. Such a lesion would certainly be painless. It would fit with the peritoneoscopic picture. I shall take a sporting chance and say they found a primary cancer of the bile ducts, with cancer of the gall bladder, the ampulla and the pancreas as the second, third and fourth choices, respectively.

CLINICAL DIAGNOSIS

Carcinoma of gall bladder

DR BREED'S DIAGNOSIS

Primary cancer of bile ducts

ANATOMICAL DIAGNOSES

Cholecystitis, chronic

Cholelithiasis

Obstruction of common duct by external pressure.

Biliary cirrhosis of the liver

Central necrosis of the liver

Bile necrosis

Arteriosclerosis

PATHOLOGICAL DISCUSSION

DR MALLORY The peritoneoscope is the latest important addition to our diagnostic armamentarium and is still too new to have been thoroughly evaluated. Its potential value is certainly great but like any other diagnostic procedure it has its limitations. Only occasionally, and then with the aid of biopsies taken through it, can it alone establish a diagnosis. In the usual case it simply gives us more items of information which must be fitted into the general pattern to establish a diagnosis. The technic of using these instruments can be readily acquired, but the eye behind the instrument is not so quickly trained. Years of experience and constant check with the operating room and the postmortem table will evidently be necessary. The number of those who actually use the peritoneoscope will probably remain small, but every clinician should gain some degree of experience in interpreting the results of peritoneoscopy. He must learn what types of observation can accurately be made by this method and what observations may legitimately be questioned if they do not fit into the general clinical picture.

This patient was explored a few days after peritoneoscopy and came to postmortem examination a week after that, so we have a double check on the peritoneoscopic observations. Dr Edward B. Benedict noted, as has been reported, that the gall bladder had markedly thickened walls of very hard consistence and also that the liver was greenish-brown and appeared to be large. At operation and at autopsy as well the discoloration was confirmed but the organ was found not to be enlarged but to be prolapsed downward. It seems fair to conclude, therefore, that peritoneoscopic examination does not give a reliable indication as to the size of the liver. Dr Benedict believed that the appearance of the gall bladder strongly suggested carcinoma and made that diagnosis. At the time of his examination he took a biopsy in which, however, we could find only chronic inflammation and no evidence of neoplasm. At exploration the surgeon likewise was of the opinion that the gall bladder was neoplastic and that the condition was essentially inoperable. Autopsy, however, proved both of them to have been mistaken in regard to the diagnosis. The gall-bladder wall was greatly thickened by fibrous inflammatory tissue and the consistence was rock hard, but the latter proved to be due to the presence of two large stones within the lumen of the organ. No bile or secretion was present, and therefore there had been no sensation of fluctuation. A third stone was found in the ampulla and first portion of the cystic duct, and pressure from this and from the surrounding inflammatory tissue had

evidently partially obstructed the common bile duct from without.

Despite the absence of cancer it is very doubtful if a cholecystectomy would have prolonged this patient's life. Examination of the liver showed very extensive hepatic degeneration and considerable biliary cirrhosis. The kidneys showed a marked grade of bile nephrosis and it seems very improbable that she could have withstood an extensive operation. Two months or even one month earlier it would, of course, have been a different story.

CASE 25402

PRESENTATION OF CASE

A fifty-five-year-old musician was admitted to the hospital complaining of frequent attacks of chest pain.

About ten weeks before entry the patient had been given a colonic irrigation for constipation. During the procedure he developed, for the first time, attacks of anterior chest pain, which extended from axilla to axilla and which seemed to be centered in the right axilla. Since the onset, these attacks had recurred approximately on alternate days, with the pain characteristically beginning an hour after supper and lasting from thirty to sixty minutes unless stopped by the ingestion of nitroglycerin pills, which were usually effective. The larger the meal the sooner the discomfort began. The pains were not related to exertion or fatigue and did not radiate down the arm. There was no associated palpitation or breathlessness. His last attack occurred the evening before admission. He had taken digitalis daily, but the amounts and length of time of dosage were not stated.

Nineteen years before admission the patient had had an alleged attack of rheumatic fever. There were no subsequent attacks, but since then he had had sore throats. Eleven years before entry his tonsils were treated with an electric needle without any particular improvement, and two years later he had a tonsillectomy. The patient had been worrying about his heart because of palpitation. Four years before admission because of throbbing headaches and hypertension, he had a 600-cc phlebotomy performed, without complication.

The family and marital histories were not contributory.

The physical examination revealed a slightly obese man who did not appear ill. The vessels of the fundi were slightly tortuous. The left border of dullness of the heart was percussed 11 cm beyond the midsternal line, with the right border

at the sternum. The supracardiac dullness measured 5 cm. The sounds were of poor quality and extrasystoles were heard every three or four beats. There was a questionable gallop rhythm, and a soft systolic murmur at the apex. The blood pressure was 250 systolic, 125 diastolic. The lungs were clear. The remainder of the examination was essentially negative. The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 5,090,000 with 100 per cent hemoglobin (Sahli), and a white-cell count of 10,000 with 67 per cent polymorphonuclears.

The temperature, pulse and respirations remained essentially normal throughout his hospital stay. He was comfortable and without precordial pain until the evening of the fifth hospital day when he developed substernal pain, which lasted over ninety minutes and which was only slightly relieved by four tablets of nitroglycerin. With the onset of the pain he became gray but not cyanotic, the heart sounds were of poor quality, but the rhythm was regular at 72 beats per minute. The blood pressure was 150 systolic, 100 diastolic. He was mentally clear. A few hours later the blood pressure rose to 190 systolic, 110 diastolic, and although he showed no signs of shock and was not cyanotic, he quickly failed and died in the early morning of the sixth hospital day about eight hours after the onset of the attack.

DIFFERENTIAL DIAGNOSIS

DR HOWARD B. SPRAGUE. Of course the prominent pieces of evidence in this case are the story of known hypertension for at least four years before the final episode and the finding of a blood pressure recording of 250 systolic, 125 diastolic. The question is, What else did he have besides high blood pressure? His attacks of pain started ten weeks before his death and the first one came in relation to a colonic irrigation. That is rather interesting. We know that stimulation by distention of the upper intestinal tract can precipitate attacks of angina pectoris, but this story is certainly not the common way in which the intestinal tract is distended as a precipitant. It is furthermore rather atypical that subsequent attacks were not related to exertion but came regularly after supper on alternate days, with the discomfort lasting a half hour to an hour unless he took nitroglycerin which usually was effective. One usually thinks that episodes of such long duration are not ordinary attacks of angina pectoris but I think that the discomfort which comes in patients with coronary disease after meals may have a much longer duration perhaps go-

ing and coming somewhat over this period of time and still be considered a coronary symptom. Nitrites do have an effect on relaxation of the gastrointestinal tract, specifically the pyloric sphincter, and there may be some relation here between referred discomfort from the stomach and the coronary type of pain. The nitroglycerin might have an effect on both of them to some degree. One thinks, of course, because of this particular sort of relation to meals, about the question whether there was something else there, such as gall-bladder disease, which complicated the situation.

He had in his past history, so far as the cardiovascular system is concerned, a story of a questionable attack of rheumatic fever and on physical examination had a systolic murmur at the apex. Perhaps this is unimportant, although it is possible we may find some slight, healed rheumatic involvement of the mitral valve. The physical findings are consistent with hypertension, in that the vessels of the fundi were slightly tortuous. The poor quality of the heart sounds, the questionable gallop rhythm and terminal cardiac failure, with normal rhythm except for the premature beats, were apparently due not to congestive failure but to anginal failure. The final episode consisted of substernal pain, lasting for an hour and a half and only slightly relieved by repeated nitroglycerin. There seems to be little question but that he had an occlusive episode—he became gray at the time of the severe pain and there was a drop in his blood pressure to 150 systolic, 100 diastolic, with a later recovery to 190 systolic, 110 diastolic. Is that the final blood-pressure recording?

DR BENJAMIN CASTLEMAN Yes.

DR SPRAGUE Unless there is something else in this picture that I cannot see, we seem to be dealing with hypertensive coronary disease with a final attack of coronary occlusion. Perhaps we might even speculate further about this angina pectoris which he had with substernal pressure. It seems to have centered in the right axilla. As it was related to the change in position of the diaphragm and was especially brought on by colonic irrigation, it makes me think that the chief lesion might be in the right coronary artery rather than the left. There is not, in my experience, a very good correlation between radiation of pain to the right and involvement of the right coronary artery and usually, of course, both coronaries are involved but some evidence points in this direction.

There is one other point in relation to the character and position of pain brought on by colonic irrigation. I have seen several patients with acute

attacks of colonic diverticulitis whose attacks simulated coronary thrombosis with severe epigastric pain, vomiting and collapse. I think we have nothing to suggest that here. I shall say then that he had hypertensive coronary heart disease, angina pectoris and terminal coronary occlusion. The latter was not of long enough duration to have caused obvious cardiac infarction—although he lived for eight hours—and possibly involved chiefly the right coronary artery.

DR PAUL D WHITE Dr Sprague referred to the strong possibility that trouble with the digestive tract might have caused the symptoms at the beginning, after colonic irrigation. I should favor that too. There was no relation between the pain and exertion, but the pain did come after the first colonic distention and then with meals after that. Whether there was gall-bladder disease or simply an irritability of the gastrointestinal tract with cardiospasm or distention of the colon, I do not know, but I should favor the diagnosis of indigestion. Terminally we must also think of a dissecting aortic aneurysm and pulmonary embolism, because they crop up sometimes when we least expect them. Although I should agree that coronary thrombosis is the most likely diagnosis, I should put second a dissecting aortic aneurysm, and third, pulmonary embolism.

CLINICAL DIAGNOSIS

Hypertensive coronary heart disease, with angina pectoris, coronary occlusion and cardiac failure.

DR. SPRAGUE'S DIAGNOSES

Hypertensive coronary heart disease
Angina pectoris
Terminal coronary thrombosis (? right coronary artery)

ANATOMICAL DIAGNOSES

Coronary thrombosis, old, right main and left circumflex, recent, first branch of left descending
Cardiac infarction, old, left ventricle
Pulmonary edema, massive, bilateral
Pleuritis, chronic fibrous, right
Hydrothorax, slight, bilateral
Nephritis, chronic vascular
Polypi of colon
Cardiac hypertrophy and dilatation, hypertensive type
Slight rheumatic heart disease, aortic valve
Atherosclerosis, marked, coronary and aortic
Prostatic hyperplasia, slight

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN This man did have a large hypertensive heart, weighing 700 gm. We found no evidence of fresh infarction, but at the apex there was a healed scar measuring a little over 1 cm. in diameter, evidence of a previous infarction. Examination of the coronaries showed that the right and left were both markedly involved with arteriosclerosis. They were thickened and calcified. The right coronary, about 6 cm. from its origin, was completely occluded by an old organized thrombus, the lumen on either side of which was very narrow, almost pinpoint. The circumflex branch of the left, a few centimeters from its origin, was also occluded by a similar old and organized thrombus. A small branch of the main descending branch of the left contained a fresh thrombus.

A section of the latter shows a narrow media, apparently compressed by thick fibrous intimal proliferation. Within the intima is an area of hemorrhage, all the way around the vessel. In one spot is a rupture of the intima with hemorrhage into the lumen, which apparently preceded the thrombosis. This fits in with the Paterson* theory that rupture of an internal hemorrhage is the most frequent precipitating cause of coronary thrombosis. We cut our section through an area that shows it very well. Most of the material within the lumen is a hemorrhagic thrombus with no atheromatous necrotic deposits. Another interesting feature of the slide is that the

media and part of the adventitia are diffusely infiltrated with acute and chronic inflammatory cells—eosinophils, plasma cells and lymphocytes. I am not sure that pure arteriosclerosis can cause such an extensive irritation to produce that amount of infiltration secondarily. It is possible that this could be a rheumatic arteritis or something like that, which may have predisposed this vessel to thrombosis.

DR. WHITE A periarthritis?

DR. CASTLEMAN No, there was no periarthritis.

The mitral valve was slightly thickened and showed a very slight but definite amount of rheumatic endocarditis. The aorta showed a severe degree of arteriosclerosis. The kidneys weighed 200 gm. and showed a moderate degree of vascular nephritis. The lungs were markedly congested and edematous and contained a few foci of bronchopneumonia.

DR. WHITE Was there any gall-bladder disease?

DR. CASTLEMAN No.

A PHYSICIAN Can the pain which was related to meals and not due to exertion or fatigue be explained?

DR. SPRAGUE In certain cases of angina pectoris I think it is striking that there is a specific excitant for the individual which is much more impressive than are some others. I do not know how much effort he was put to in his ordinary life. Perhaps more physical exertion might have precipitated anginal attacks. It is not known what instrument he played; some require more exertion than others.

*Paterson, J. C.: Vascularization and hemorrhage of the intima of arteriosclerotic coronary arteries. Arch. Path. 22:313-324, 1916.

The New England Journal of Medicine

Formerly the

Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

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THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

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SUBSCRIPTION TERMS \$6.00 per year in advance postage paid for the
United States Canada \$7.04 per year \$8.52 per year for all foreign coun-
tries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon
on Saturday

THE JOURNAL does not hold itself responsible for statements made by any
contributor

COMMUNICATIONS should be addressed to the *New England Journal of
Medicine* 8 Fenway Boston Mass

SALVATION ARMY APPEAL

IN response to the 1939-40 Greater Boston Annual Maintenance Appeal of the Salvation Army there will come to the aid of that organization, as heretofore, big-hearted men and women of the business world, as well as many folk who are charitably inclined. With a determination in the minds and hearts of the workers—the Salvation Army officials—and the campaign organization that the “Door of Service” must be kept open, the appeal will get underway on October 9, with a luncheon at the Boston Chamber of Commerce.

Its goal is set at \$195,000 and includes \$25,000 which will be raised by sponsoring groups in corps towns of Cambridge, Chelsea, Everett, Malden, Medford and Somerville. The arrangement is made so that campaigns in these cities will run simultaneously with the Boston activities, thus

giving added impetus to the drives. In Boston proper the amount to be raised is increased over last year's goal by \$15,000. This is the approximate amount to be set aside each year for the operation and maintenance of the Salvation Army's new unit,—The South End Boys Club,—which was a gift of the Charles Hayden Foundation. The building operation is in progress at Washington and East Canton streets, on a site adjoining the New England headquarters and the Palace Hotel of the Salvation Army. When the building is completed, the block fronting on Washington Street and backing on Mystic Street, from East Brookline Street to East Canton Street, will represent one of the largest character-building centers in this part of the world.

The quota set represents money that is needed to keep in active state the many units and avenues of service that are well known to Greater Boston folk. It means keeping the “Door of Service” open for friendless men and women and for lonesome or backward boys and girls. In speaking of the work of the Salvation Army, Colonel Edmund C. Hoffman, chief executive in New England, said “If you are in trouble it makes no difference who you are or from where you come. The Salvation Army gives a helping hand regardless of race, color or religion.” This charitable organization deserves the support of the medical profession!

SMALLPOX INCREASES

MASSACHUSETTS has reason to be proud of its splendid record of almost universal vaccination against smallpox. This fact is emphasized by a recent report of the United States Public Health Service* on the prevalence of smallpox in this country. In 1934 the disease had dropped to a low level of only slightly above 5000 cases. Since then there has been a rapid increase, reaching 11,673 cases in 1937 and almost 15,000 in 1938.

At this level the United States is leading all the nations in the world except India in the incidence of the disease. “In 1936 [last available world-

*Where and why smallpox is occurring in the United States. Pub. Health Rep. 54:1091-1093, 1939.

wide figures], according to reports of the Health Organization of the League of Nations, England and Wales, with a population of 40,839,000, reported only 12 cases. France, with 41,906,000 population reported 273 cases and Germany, with a population of 67,346,000 reported no cases."

Massachusetts has not contributed a single case toward this high smallpox record. The last case reported in the State occurred early in 1932. This record would not have been possible without the continued efforts of physicians and health workers during the last hundred years. In 1809 less than ten years after vaccination was introduced into the State, a law was passed making it mandatory that each community appoint a committee to have charge of vaccination. At that time the virus was propagated by the arm-to-arm method and unless someone had the responsibility of the continuous transference of cowpox, the virus was not available for an emergency. For a time smallpox almost disappeared and in 1837 the law was repealed. A gradual increase in unvaccinated individuals resulted, and by 1853 smallpox had become so prevalent that the legislature passed our present compulsory vaccination law.

At first the vaccination law was very poorly enforced, and by 1871 a large unvaccinated population had again accumulated and a sharp outbreak, centered around Boston, occurred. Better enforcement of the law ensued, and the disease remained at low levels for several years. It took another outbreak in 1901 to stimulate universal observation of the law, and since that time smallpox has never again obtained a foothold in the State. In spite of this splendid record we have to defend our vaccination law against repeal at every session of the legislature.

Massachusetts is not the only state which has not contributed to the high smallpox record. A score of states along the Atlantic seaboard in which the practice of vaccination is popular have had very few cases. Five of them have not had a single case during the last five years.

The high national record is due largely to the prevalence of the disease in the states of the Great Plains and the Pacific Northwest. In some of

the states, notably North and South Dakota, Utah, Wyoming, Oregon and Idaho the case rate is among the highest reported anywhere in the world. This is the area in which vaccination is most neglected. Of the thirteen states that have compulsory vaccination laws and of the fourteen that permit local option only two and four, respectively, are west of the Mississippi.

It cannot be expected that Massachusetts will continue indefinitely to report no cases of smallpox. Eventually someone in the incubation period of the disease will come into the State and become ill here, or a missed case of the disease will cross the border and infect susceptible individuals. We can feel secure, however, in the knowledge that only a few cases can occur because practically everyone in the State has been vaccinated.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY *

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

SEPTIC ABORTION FOLLOWING CURETTAGE

Mrs. D., a twenty-three year-old white woman, was admitted to the hospital on April 7, 1911. On March 28 her expected catamenia failed to appear and on March 30 a catheter was passed into the uterus in order to produce an abortion. Two days later she started to flow, felt feverish and vomited. These symptoms continued and the patient was sent to the hospital.

The family history was not taken. The patient's past history was uneventful. She had had one spontaneous delivery at term ten months previously the pregnancy and puerperium had been normal. Catamenia began at fifteen were always somewhat irregular usually lasted eight days and were painless.

Examination showed a well-developed and nourished woman who did not look very sick. The tongue was moist and slightly coated. The temperature was 101 F., and the pulse 94 and of good quality. The heart showed slight enlargement to the right and there was a loud blowing systolic murmur which was heard over the

A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

precordium and transmitted to the axilla. The breath sounds were clear, and resonance was uniform over the whole chest. The abdomen was tender throughout, markedly so in the left lower quadrant, but there was no spasm.

On vaginal examination the cervix was found to be soft and patulous. The uterus was retroflexed, and the body soft and tender, the exact size could not be determined because of the tenderness. The vaults were somewhat tender, but no masses were palpated. There was a moderate discharge of bloody mucus from the vagina.

The following morning the temperature rose to 102°F and curettage was decided on. Under ether anesthesia the cervix was dilated and the uterus curetted of a small amount of tissue which showed no chorionic villi or decidual cells on microscopic examination. A culture taken from the uterus showed no growth. The uterus was washed out before and after the curettage with 70 per cent alcohol, and a gauze strip saturated with iodine was left in the uterus for two hours.

The temperature remained elevated, fluctuating between 100 and 103°F, and the patient grew steadily worse. A blood culture taken on the fourth day after the curettage showed no growth. The white count at that time was 32,000, the hemoglobin 80 per cent. The pulse steadily climbed in rate and decreased in quality. The respirations also increased in rapidity, and a cough developed. Rales appeared in both chests, but there were no signs of consolidation. The abdomen became distended and rigid, and vomiting continued.

On the tenth day following curettage the temperature fell, the pulse became imperceptible, and the respirations rose to between 40 and 50. She represented the picture of severe general sepsis in extremis. Death occurred at six o'clock in the afternoon.

An autopsy showed purulent peritonitis, purulent salpingitis, purulent endometritis, atelectasis of both lungs, septic adrenal glands, dilatation of the right side of the heart, septic spleen and cloudy swelling of the kidneys.

Comment. The most important point in this case was the injudicious and probably harmful use of the curet in uterine infection. At the time when this patient was treated it was customary with many obstetricians to curette all patients with uterine sepsis, whether complicating miscarriage or full term delivery. The harmful effects of this procedure are now recognized, and today this patient would have been treated more conservatively.

In this case the fact that the patient had skipped her period only ten days previously was entirely

ignored, in this early period of gestation there was obviously but little tissue that could have been removed by the curet. Furthermore, there is no proof that this patient was pregnant. Neither the tissue removed at curettage nor the autopsy findings revealed evidences of pregnancy. This brings out another point of importance, namely, that the introduction of a catheter or other instrument into the uterus in the attempt to produce an abortion may result in severe and fatal infection even when the woman is not pregnant.

DEATHS

BAKER—FREDERICK H. BAKER, M.D., of Worcester, died October 1. He was in his seventy-third year.

Born in Billerica, he attended the public schools there and received his degree from the Harvard Medical School in 1893. In 1894 he established the first diagnostic laboratory in Massachusetts at the Worcester City Hospital. The following year he was appointed medical examiner for the Eleventh District, a position which he held for forty-two years. Dr. Baker was director of laboratories at Memorial Hospital and Worcester State Hospital and was chief pathologist at the Worcester City Hospital. For thirty years he was head of the medical department at Clark University.

He held memberships in the American Medical Association and the Massachusetts Medical Society, being a former president of the Worcester District Medical Society. He was also a former president of the Massachusetts Medical Examiners Society.

His widow, two brothers and two sisters survive him.

BREWSTER—GEORGE W. W. BREWSTER, M.D., of Boston, died September 26. He was in his seventy-fourth year.

Born in Roxbury, he attended Roxbury Latin School, graduated from Harvard University in 1889 and received his degree from the Harvard Medical School in 1893. Dr. Brewster served his internship at the Massachusetts General Hospital and was a member of its staff from 1901 to 1926, being named a member of the board of consultation in the latter year.

He was a fellow of the Massachusetts Medical Society, the American Medical Association and the American College of Surgeons. He held memberships in the American Surgical Association, the New England Surgical Society, the Boston Surgical Society, the International Surgical Society and the Aesculapian Club.

His widow and three sons, William L., George W. W., and Dr. Henry H. Brewster, survive him.

FITCHET—SETH M. FITCHET, M.D., of Newton Center, died September 26. He was in his fifty-third year.

Born in San Bernardino, California, he attended Mount Hermon School, Northfield, and graduated from Clark University, Worcester. He received his degree from the Harvard Medical School in 1921 and a B.P.H. from the Harvard School of Public Health two years later.

Dr. Fitchet had served as surgeon in the Department of Hygiene at Harvard University, assistant surgeon at the Massachusetts General Hospital, consultant at the Massachusetts Eye and Ear Infirmary, and visiting surgeon at the Children's, New England Baptist and Faulkner hospitals.

His fellowships included the Massachusetts Medical Society American Medical Association and the American College of Surgeons. He was a member of the Boston Orthopaedic Club and the Aesculapian Club.

His widow, two sons and a daughter survive him.

JORDAN—MICHAEL M. JORDAN, M.D., of Worcester died September 30. He was in his fifty-sixth year.

Born in Wayzata, Minnesota, he received his degree from the University of Minnesota College of Homeopathic Medicine and Surgery in 1905. The following year he joined the staff of the Westboro State Hospital as a psychiatrist. He was a member of the staffs of the Worcester City and St. Vincent hospitals and was a consultant at the Hahnemann Hospital. Dr. Jordan had been connected with the State Industrial Accident Board for many years.

Dr. Jordan held fellowships in the Massachusetts Medical Society and the American Medical Association. He was a member of the American Psychiatric Association, the New England Society of Psychiatry and a diplomat of the American Board of Psychiatry and Neurology.

His widow, a son, two daughters and several brothers and sisters survive him.

LUCE—LEROY A. LUCE, M.D., of Boston died September 27. He was in his sixty-first year.

Born in Randolph, Vermont, he attended Tufts College Medical School, receiving his degree in 1906. He started practice in Boston and spent a great deal of time in developing a sine-wave machine for use in the treatment of infantile paralysis.

Dr. Luce was a fellow of the Massachusetts Medical Society and the American Medical Association and held memberships in the American Psychiatric Association and the New England Society of Psychiatry.

He was unmarried. A niece survives him.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST 1939

DISEASES	AUGUST 1939	DECEMBER 1938	FIVE YEAR AVERAGE
Anterior poliomyelitis	15	4	130
Chickenpox	121	99	101
Diphtheria	13	8	23
Dog bit	1208	1110	1077
Dysentery bacillary	12	22	38
Eczema	16	34	42
Gonorrhea	432	433	542
Lobar pneumonia	78	137	119
Measles	282	258	164
Meningococcus meningitis	2	4	5
Mumps	81	143	100
Paratyphoid B fever	3	10	9
Scarlet fever	83	125	151
Syphilis	367	422	451
Tuberculosis, pulmonary	316	320	399
Tuberculosis, other forms	27	37	35
Typhoid fever	11	11	15
Undulant fever	0	5	4
Whooping cough	440	399	501

Based on figures for preceding five years.

RARE DISEASES

Anterior poliomyelitis was reported from Adams, 1 Boston, 1 Brockton, 1 Everett, 3 Malden, 3 Newton, 2 Templeton, 1 Wellesley, 1 Winchester, 1 Worcester, 2 total 15.

Diphtheria was reported from Boston 5 Cambridge, 1 Fall River, 1 Gloucester, 1 Lawrence, 1 Malden, 1 New Bedford, 2 Watertown, 1 total 13.

Dysentery, amebic, was reported from Springfield, 1 Worcester, 1 total, 2.

Dysentery bacillary, was reported from Belmont, 1 Boston, 3 Canton, 2 Chelsea, 1 Conway, 1 Danvers, 2 Fall River, 1 Worcester, 1 total, 12.

Infectious encephalitis was reported from Westfield, 1 total 1.

Malaria was reported from Newton, 1 Worcester, 1 total 2.

Meningococcus meningitis was reported from Northbridge, 1 Worcester, 1 total, 2.

Paratyphoid B fever was reported from Boston, 1 Lynn, 1 West Stockbridge, 1 total, 3.

Pellagra was reported from Boston, 1 Brockton, 1 total 2.

Septic sore throat was reported from Belmont, 1 Boston, 2 Everett, 1 Fall River, 1 total 5.

Tetanus was reported from Longmeadow, 1 Pepperell, 1 South Hadley, 1 total 3.

Trachoma was reported from Malden, 1 total 1.

Typhoid fever was reported from Boston, 2 Lowell, 1 Malden, 1 New Bedford, 1 North Reading, 1 Quincy, 3 Somerville, 1 Springfield, 1 total 11.

Anterior poliomyelitis continued to show low incidence. Pulmonary tuberculosis, measles, and chickenpox were reported above the five year average.

Scarlet fever showed record low incidence for this or any other month.

The incidences of meningococcus meningitis and undulant fever were not remarkable.

Tuberculosis (other forms) was reported at a record low figure.

Lobar pneumonia, whooping cough, mumps, diphtheria and German measles were reported below the five year average.

Typhoid fever was reported at record low figures except for the years 1937 and 1938 which were equalled.

The reported incidence of dog bite showed a record high figure. Animal rabies showed record low incidence. Foci in the vicinity of Franklin and Foxborough were active.

CORRESPONDENCE

AGENCIES AND INDIVIDUALS ENTITLED TO RECEIVE INFORMATION PERTAINING TO GONORRHEA AND SYPHILIS

To the Editor: Physicians frequently request information from this department as to who is entitled to information concerning infection with syphilis or gonorrhea in their patients.

The list of individuals and agencies that under the law are entitled to such information on demonstration of good faith has recently been revised to meet modern requirements and is appended.

PAUL J. JAKMAUTH, M.D.,
Commissioner of Public Health

State House,
Boston.

Under the provisions of the General Laws, Chapter 111, Section 119, the Commissioner of Public Health has declared that the following agencies and individuals are entitled on demonstration of good faith to receive information from hospital dispensary laboratory and morbidity reports pertaining to gonorrhea or syphilis. "Demonstration of good faith" is intended to mean that the agency or individual desiring the information intends to

use it to the patient's advantage and not merely to satisfy curiosity or to the patient's disadvantage, except as health officers or other officials may be obliged to control the patient for the protection of the public health

NATIONAL, STATE AND MUNICIPAL AGENCIES AND OFFICERS

- 1 Boards of health and health officers
- 2 Departments of correction (parole officers)
- 3 Departments of education (physicians, nurses and divisions of blind)
- 4 Departments of industrial accidents
- 5 Departments of mental diseases
- 6 Departments of probation (probation officers)
- 7 Departments of soldiers' relief
- 8 Departments of public welfare (divisions of aid and relief)
- 9 Hospitals
- 10 Other institutions (superintendents and physicians)
- 11 Genitoinfectious disease clinics
- 12 National Guard (Medical Corps)
- 13 U S Army, Navy, Marines (Medical Corps)
- 14 U S Department of the Interior (Bureau of Pensions)
- 15 U S Veterans' Bureau
- 16 U S Public Health Service

PRIVATE AGENCIES AND INDIVIDUALS

- 1 Hospitals
- 2 Physicians, for cases in their own private practices only
- 3 Industries (physicians only)
- 4 Private schools (physicians only)
- 5 Visiting nurse associations (incorporated associations only, having at least one full time nurse)
- 6 Child welfare and child placing agencies (incorporated agencies only, having at least one full time nurse or social worker)
- 7 Family welfare agencies (incorporated agencies only, having at least one full time social worker or nurse)
- 8 American Red Cross (only those chapters having at least one full time social worker or nurse)
- 9 Florence Crittenton League and Welcome House
- 10 The patient or his guardian

EXECUTORS OR ADMINISTRATORS OF ESTATES

Only on the presentation by said executor or administrator of a reasonable need for the information, said evidence of reasonable need to be satisfactory to the agency from which the information is requested

INSURANCE COMPANIES

- 1 If the beneficiary of the insurance is living (as in compensation insurance, accident insurance, and so forth) a copy of the patient's record may be given or sent to the patient, himself at his request, or if he be a minor, to his parent or legal guardian. The patient may then divulge the record to the insurance company or not as he sees fit.
- 2 If the patient is deceased (in the case of life insurance, and so forth), a copy of the patient's record may be given or sent to the beneficiary who may then divulge the information to the insurance company or not

as he sees fit. Presumably the identification of the beneficiary applying for the record may be established by the insurance company, preferably in writing

Any agency or individual not included within the provisions of this list may receive information concerning syphilis and gonorrhea on court order only

PAUL J JAKMAUH, M.D.,
Commissioner of Public Health

June, 1939

DENTISTRY'S PLACE IN THE NATIONAL HEALTH PROGRAM

To the Editor In the latter part of June, an invitation was extended to the members of the Massachusetts Medical Society, through its secretary, to attend a meeting of the Metropolitan District Dental Society, at the Hotel Vendome, Boston, on Wednesday, October 25. At this time, Dr. R. M. Walls, chairman of the Economic Committee of the American Dental Association, is to present a timely paper on "Dentistry's Place in the National Health Program." Are the members of the Massachusetts Medical Society interested in socialized dentistry? How will they be affected if the Wagner Act is passed in its present form? They should come and hear Dr. Walls, and have their questions answered by him.

Dinner will be served at six o'clock at \$1.50 per plate. It will be appreciated if members wishing to attend the dinner will send their reservations accompanied by checks to the Executive Office, 106 Marlborough Street, Boston, not later than October 24, so that proper covers and seating arrangements at the meeting will be provided for all. Make checks payable to the Metropolitan District Dental Society. Members of the Massachusetts Medical Society will be welcome to hear the speaker at about eight o'clock if they do not wish to attend the dinner.

EDWIN J MORSE, *Secretary*
Metropolitan District Dental Society

106 Marlborough Street,
Boston

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor In addition to the articles enumerated in our letter of August 11 the following have been accepted

Abbott Laboratories

Tablets Cevitamic Acid — Abbott, 0.05 gm

Parke, Davis & Co

Ampules Adrenalin in Oil, 1 cc

Riedel-de Haen, Inc.

Ampules Solution Decholin-Sodium, 20 per cent, 3 cc.

Sharp & Dohme

Immune Globulin (Human)

Smith-Dorsey Co

Tablets Nicotinic Acid, 50 mg

Tablets Ascorbic Acid, 25 mg

Frederick Stearns & Co

Stearns Viosterol (ARPI Process) in Oil

Stearns Cod Liver Oil Concentrate in Vegetable Oil

Stearns Cod Liver Oil Concentrate Capsules,
3 min

Stearns Cod Liver Oil Vitamin Concentrate Tablets
 Stearns Halibut Liver Oil Plain
 Stearns Halibut Liver Oil Plain Capsules, 3 min.
 Stearns Halibut Liver Oil with Viosterol (A.R.P.I. Process)
 Stearns Halibut Liver Oil with Viosterol (A.R.P.I. Process) (with other fish liver oils) Capsules

The following product has been accepted for inclusion in the "List of Articles and Brands Accepted by the Council But Not Described in N.N.R." (*New and Nonofficial Remedies* 1939 p. 528)

The Emergency Antidote Kit Company
 Emergency Antidote Kit (Jacobson)

PAUL NICHOLAS LEECH *Secretary*

535 North Dearborn Street,
 Chicago Illinois.

NOTICES

REMOVALS

J. L. GRUND, M.D., announces the removal of his office to 520 Beacon Street, Boston.

MICHAEL E. MCGARTY, M.D. announces the removal of his office from 312 Beacon Street, Boston to 131 Bay State Road, Boston.

FRANKLIN S. NEWELL, M.D., announces the removal of his office to 330 Dartmouth Street, Boston

JOHN L. NEWELL, M.D., announces the removal of his office to 330 Dartmouth Street, Boston.

HERBERT SHERWIN, M.D. announces the removal of his office to 483 Beacon Street, Boston.

BOSTON CITY HOSPITAL

The monthly clinicopathological conference will be held at the Boston City Hospital on Wednesday October 11 at 12 o'clock noon in the Pathological Amphitheater

JOSEPH E. HALLISEY, M.D., *Secretary*
 Medical Staff

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Jacobus Langendoen of the Boston Symphony Orchestra every Thursday at 8.30 p.m., beginning October 19. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel Brookline (BEA 2430)

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association 554 Columbus Avenue, Boston on Tuesday October 17 at 12 o'clock noon. Dr. Leland S. McKittick will speak on "The Diagnosis and Treatment of Acute Intestinal Obstruction."

Physicians are cordially invited to attend.

JOHN B. HALL, M.D. *Secretary*

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic on abdominal pain will be conducted by Drs. Elliott Cutler and Soma Weiss on Wednesday October 11 at 2:00 p.m. A clinicopathological conference, conducted by Dr. Cutler will follow

Physicians and students are cordially invited to attend

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
 Lecture Hall 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

Friday October 6—Medico-Legal Aspects of Heart Disease. Dr. S. A. Levine.
 Saturday October 7—Hospital Case Presentation. Dr. S. J. Thannhauser
 Tuesday October 10—Oral Infection and Its Sequelae. Dr. R. H. Norton.
 Wednesday October 11—Hospital Case Presentation. Dr. S. J. Thannhauser
 Friday October 13—The Care and Diagnosis of Head Injuries During Their Convalescence. Dr. Donald Munro
 Saturday October 14—Hospital Case Presentation. Dr. S. J. Thannhauser
 Tuesday October 17—Allergy Clinic. Discussion of some histories and cases. Dr. E. A. Brown
 Wednesday October 18—Non-Hemolytic Familial Jaundice. Dr. William Dameshek.
 Thursday October 19—Hospital Case Presentation. Dr. S. J. Thannhauser
 Friday October 20—Heredity and Environment in Relationship to Intelligence, Personality and Mental Disease. Dr. Abraham Myerson
 Saturday October 21—Hospital Case Presentation. Dr. S. J. Thannhauser
 Tuesday October 24—Endocrine Clinic. Dr. C. H. Lawrence.
 Wednesday October 25—Hospital Case Presentation. Dr. S. J. Thannhauser
 Thursday October 26—Ventricular Fibrillation as the Mechanism of Sudden Death in Patients with Coronary Occlusion. Dr. Henry Miller
 Friday October 27—Title to be announced. Dr. A. O. Hampton
 Saturday October 28—Hospital Case Presentation. Dr. S. J. Thannhauser

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday October 10 in the amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance) at 8:15 p.m.

PROGRAM

Presentation of cases.

A New Surgical Method to Improve the Blood Supply to the Heart in Coronary Disease. Dr. Mercier Fauteux, of Montreal clinical assistant in surgery Royal Victoria Hospital.

Medical students and physicians are cordially invited to attend.

ROBERT M. ZOLLINGER, M.D., *Secretary*

FIFTH POSTGRADUATE SEMINAR IN NEUROPSYCHIATRY

The Metropolitan State Hospital, Waltham, recently announced the opening of the Fifth Postgraduate Seminar in Neuropsychiatry.

The course consists of two units: neurology, October 2 to December 19, and psychiatry, January 8 to March 25. It is designed as a comprehensive review course, not only for physicians preparing for the examinations of the American Board of Psychiatry and Neurology, but for those desirous of additional training in the specialty. The teaching staff comprises a number of recognized specialists in this field throughout the state and is under the direction of Dr. Roy D. Halloran, superintendent, Metropolitan State Hospital, and Dr. Paul I. Yakovlev, clinical director, Walter E. Fernald State School.

SUFFOLK DISTRICT MEDICAL SOCIETY

A meeting of the Suffolk District Medical Society will be held at the Boston Medical Library, 8 Fenway, on Wednesday, October 25, at 8:15 p.m.

PROGRAM

Stated meeting

Scientific meeting

Obesity and Menstrual Disturbance: Endocrine and endometrial studies. Drs. Charles H. Lawrence, Joseph T. Smith and Nicholas T. Werthessen.

Clinical Studies in Primary Malignancy of the Lung. Dr. Richard H. Overholt.

Xanthomatosis. Dr. Siegfried J. Thannhauser.

Observations on Heart Disease. Dr. Samuel H. Proger.

Secretin Test of Pancreatic Function. Dr. Joseph H. Pratt.

REGINALD FITZ, M.D., *President*,

MILTON H. CLIFFORD, M.D., *Secretary*

NEW ENGLAND DERMATOLOGICAL SOCIETY

The next regular meeting of the New England Dermatological Society will be held in Hartford, Connecticut, on Wednesday, October 18. Members of the society are invited to luncheon at the Municipal Hospital at 1:45 p.m., following which cases will be demonstrated. Dinner will be held at the Wampanoag Country Club.

Reservations for transportation will be accepted at once by the secretary, Dr. Bernard Appel, 483 Beacon Street, Boston.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The New England Society of Physical Medicine announces the election of the following officers for the year 1939-1940: Dr. Henry A. Tidgell, of Wrentham, president; Dr. George B. Carr, of Lynn, first vice-president; Dr. David T. Percy, of Arlington, second vice-president; Dr. William D. McFee, of Boston, secretary; Dr. Howard Moore, of Boston, treasurer; Drs. Charles W. McClure, of Boston, John L. O'Toole, of Haverhill, Charles W. Bruninghaus, of Worcester, A. Carleton Potter, of Boston, William G. Curtis, of Wollaston, and Claude L. Pavzant, of Boston, counselors.

FOUR COUNTY MEDICAL SOCIETY

The annual meeting of the Four County Medical Society, comprising the district societies of Berkshire, Frank-

lin, Hampden and Hampshire, will be held on Tuesday, October 10, in the auditorium of the Springfield Museum of Fine Arts, 49 Chestnut Street, Springfield. The meeting is scheduled for 9:30 a.m.; luncheon will be served at the Hotel Stonehaven at 1:00 p.m., following which Dr. Walter G. Phippen will speak briefly.

The meeting will be in the form of a symposium, "Pain: Its significance in diagnosis and prognosis." Dr. Lewis M. Hurxthal will discuss the viewpoint of general medicine; Dr. Arthur W. Allen, general surgery; Dr. Joe V. Meigs, obstetrics and gynecology; and Dr. Foster Kennedy, neurology.

All physicians of Western Massachusetts are welcome to attend.

GEORGE L. SCHADT, M.D., *President*,
W. FENN HOYT, M.D., *Secretary*

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, OCTOBER 9

TUESDAY, OCTOBER 10

- *9-10 a.m. Oral Infection and Its Sequelae. Dr. R. H. Norton. Joseph H. Pratt Diagnostic Hospital.
- *10 a.m.-12:30 p.m. Boston Dispensary tumor clinic.
- *8:15 p.m. Harvard Medical Society. Peter Bent Brigham Hospital (Shattuck Street entrance).

WEDNESDAY, OCTOBER 11

- *9-10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
- *12 m. Clinicopathological conference. Children's Hospital Amphitheater.
- 12 m. Monthly clinicopathological conference. Boston City Hospital Pathological amphitheater.
- *2 p.m. Joint medical and surgical clinic on abdominal pain. Peter Bent Brigham Hospital.

FRIDAY, OCTOBER 13

- *9-10 a.m. The Care and Diagnosis of Head Injuries During Their Convalescence. Dr. Donald Munro. Joseph H. Pratt Diagnostic Hospital.
- *10 a.m.-12:30 p.m. Boston Dispensary tumor clinic.

SATURDAY, OCTOBER 14

- *9-10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
- *10 a.m.-12 m. Medical staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Soma Weiss.
- *Open to the medical profession.

OCTOBER 5 — Faulkner clinicopathological conference. Page 513 issue of September 28.

OCTOBER 6-28 — Joseph H. Pratt Diagnostic Hospital Medical Conference Program. Page 545.

OCTOBER 10 — Four County Medical Society. Notice above.

OCTOBER 10 — Harvard Medical Society. Page 545.

OCTOBER 11 — Monthly clinicopathological conference. Boston City Hospital. Page 545.

OCTOBER 11 — Joint medical and surgical clinic on abdominal pain. Peter Bent Brigham Hospital. Page 545.

OCTOBER 13 — Pequot Association of Physicians. 8:30 p.m. Hotel Bartlett. Haverhill.

OCTOBER 15-20 — American Public Health Association. Page 441 issue of September 14.

OCTOBER 17 — South End Medical Club. Page 545.

OCTOBER 18 — New England Dermatological Society. Notice above.

OCTOBER 23-NOVEMBER 3 — New York Academy of Medicine. Page 977 issue of June 8.

OCTOBER 25 — Metropolitan District Dental Society. Page 544.

NOVEMBER 8-9 — New England Society of Physical Medicine in conjunction with the Academy of Physical Medicine. Hotel Kenmore Boston. Program to be announced.

DECEMBER 2 — American Board of Obstetrics and Gynecology. Page 1019 issue of June 15.

JANUARY 6-JUNE 8-11 1940 — American Board of Obstetrics and Gynecology. Page 160 issue of July 27.

MARCH 7-9 1940 — The New England Hospital Association. Hotel Statler Boston.

MAY 14 1940 — Pharmacopoeial Convention. Page 694 issue of May 25.

June 7-9, 1940—American Board of Obstetrics and Gynecology Page 1019
 issue of June 15

DISTRICT MEDICAL SOCIETY

SUFFOLK

October 25—Page 546.

November 2—Censors' meeting Page 411 issue of September 14

BOOKS RECEIVED FOR REVIEW

Radiologic Clinique du Cœur et des Gros Vaisseaux
 Ch. Laubry P. Cottinot D. Rouvier and R. Heim de
 Balzac. 2 vol., 340 pp. Paris: Masson et Cie 1939 460
 Fr. fr.

Civilization against Cancer Clarence C. Little. 150
 pp. New York and Toronto: Farrar & Rinehart, Inc.
 1939 \$1.50

Attaining Womanhood A doctor talks to girls about
 sex George W. Corner 95 pp. New York and Lon-
 don: Harper & Brothers, 1939 \$1.00

Sclerosing Therapy The injection treatment of hernia
hydrocele varicose veins and hemorrhoids Edited by
 Frank C. Yeomans 337 pp. Baltimore: The Williams
 & Wilkins Co., 1939 \$6.00

Textbook of Medical Treatment By various authors.
 Edited by D. M. Dunlop L. S. P. Davidson and J. W.
 McNeer. 1127 pp. Baltimore: The Williams & Wilkins
 Co., 1939 \$8.00

Phytotherapy in Medical Practice Hugh Morris. 276
 pp. Baltimore: The Williams & Wilkins Co. 1939 \$4.50

The International Medical Annual A year book of
treatment and practitioners' index Edited by H. Lettby
 Tidy and A. Rendle Short. Fifty-seventh year. 602 pp.
 Baltimore: The Williams & Wilkins Co. 1939 \$6.00

Asthma Frank Coke. With the collaboration of
 Harry Coke. Second edition. 266 pp. Baltimore: The
 Williams & Wilkins Co., 1939 \$4.00

Manual of Urology R. M. LeComte. Second edition
 295 pp. Baltimore: The Williams & Wilkins Co. 1939
 \$4.00.

The Harvey Lectures Delivered under the auspices of
the Harvey Society of New York 1938-1939 Series
 XXXIV 279 pp. Baltimore: The Williams & Wilkins
 Co. 1939 \$4.00

The Treatment of Rheumatism in General Practice
 W. S. C. Copeman. Third edition. 276 pp. Baltimore:
 The Williams & Wilkins Co., 1939 \$4.00

Essentials of Fevers Gerald E. Breen 273 pp. Balu-
 more: The Williams & Wilkins Co. 1939 \$3.00

BOOK REVIEWS

New and Nonofficial Remedies 1939 Containing descrip-
 tions of the articles which stand accepted by the Coun-
 cil on Pharmacy and Chemistry of the American
 Medical Association on January 1 1939. 617 pp.
 Chicago: American Medical Association 1939 \$1.50

The thirty-second annual volume of this invaluable se-
 ries contains descriptions of the articles which stand ac-
 cepted by the Council on Pharmacy and Chemistry of the
 American Medical Association as of January 1 1939. The
 volume consists of 617 pages of text and 67 pages devoted
 to a bibliographical index to proprietary and unoffical
 articles not included in the main work. The first volume
 of the series published in 1907 had 143 pages of text and
 the articles were arranged alphabetically this is in con-
 trast to the current volume of 684 pages in which the
 various articles are grouped into classes of remedies hav-

ing similar composition or actions, with a general index
 of individual articles.

The Council has omitted eight remedies from the pres-
 ent volume because of conflict with the rules governing
 the recognition of articles and a considerable number
 have been dropped because they are off the market. The
 statements concerning the action use and dosage and
 the composition standard of purity identity strength
 and physical properties of a number of articles have been
 revised. The omitted articles, as well as the original de-
 scriptions of revised articles can be found in previous
 volumes of the series. The complete series should be
 available in all the large centers of the country for ref-
 erence purposes.

The compilation includes acceptable proprietary sub-
 stances and their preparations, proprietary mixtures of im-
 portance, non-proprietary non-official articles of impor-
 tance and simple pharmaceutical preparations. Diagnostic
 reagents which are not used in or on the human body and
 protein diagnostic preparations are omitted except when
 special request has been made to the Council to determine
 the status of the article.

Every product in the book is subject to the official rules
 of the Council. Constant and critical consideration of its
 contents provides a valuable list of acceptable new prepa-
 rations for use in treatment. Noteworthy revisions are
 local anesthetics bismuth compounds organs of ani-
 mals (ovaries and parathyroid) vitamins and vitamin
 preparations and liver and stomach preparations. Of
 especial interest are the groups of serums and vaccines,
 and the brands of sulfanilamide.

The work is kept up to date by publication of descrip-
 tions in the *Journal of the American Medical Association*
 and by the issue of two supplements during the year.

Annual Reprint of the Reports of the Council on Phar-
macy and Chemistry of the American Medical Asso-
ciation for 1938 With the comments that have ap-
peared in the Journal 123 pp. Chicago: American
 Medical Association 1939 \$1.00

This small volume contains reports of the Council
 which were adopted and authorized for publication dur-
 ing 1938. There are final reports on articles rejected by
 the Council and on others omitted from *New and Non*
Official Remedies preliminary reports on remedies sub-
 mitted for consideration and supplemental reports on
 therapeutic or pharmacological problems of remedies be-
 ing investigated by the Council.

Dr. Perrin H. Long, a member of the Council, has
 written a special article on sulphydryl (accepted by the
 Council) which is of especial interest. Reports of par-
 ticular interest are those on allantoin a preparation of
 glyoxylylurea offered as a substitute for the surgical use
 of maggots on colloidal sulphur in the treatment of
 chronic arthritis, on ergonovine including a careful study
 of the relation of this newly discovered principle to ergot
 therapy in general and on picrotoxin in poisoning by the
 barbiturates.

The reports are well written and documented with the
 available literature on the subjects under discussion.

Treatment by Manipulation A. G. Timbrell Fisher. Third
 edition. 255 pp. New York: Paul B. Hoeber, Inc.,
 1939 \$3.75

This third edition represents 'thoroughly revised' and
 extensively rewritten previous editions and the addition
 of new chapters on "The Cult of Osteopathy" and "The
 Prevention of Adhesions." In the preface to the first

edition the author made special acknowledgment to Sir Arthur Keith and Sir Robert Jones and to the Medical Research Council for help and valuable suggestions.

Because of the existing extensive literature dealing with fractures and dislocations, these subjects are not especially considered. The introduction includes a short history of the art of bone setting from the time of Hippocrates to that of Hugh Owen Thomas and Sir Robert Jones, and a plea is made for more systematic teaching of the principles and practice of manipulative therapy in both undergraduate and postgraduate education.

In the chapter on "The Cult of Osteopathy" the author acknowledges his indebtedness to a recent book by Drs Charles Hill and H. A. Clegg, entitled *What is Osteopathy?* (London: J. M. Dent and Sons, Ltd., 1938). Your reviewer has read this book carefully, and believes that every "regular" physician should read it. Although it is a scathing and convincing indictment of the lack of any scientific basis of the cult, it is a fair and factual presentation of this American born system of therapy. Fisher's chapter touches the high points of this valuable volume of Drs Hill and Clegg, and is an excellent *aperitif* for the hearty meal which their book offers.

Fisher classifies the cases appropriate for medical manipulation into four types, which often present combinations: cases with adhesions, functional or hysterical cases, unreduced dislocations or subluxations, and miscellaneous groups. The cases with adhesions are again subdivided into intra-articular, articular and periarticular groups. The functional or hysterical cases are divided as follows: a purely functional group, a group originally functional but complicated by long disease, a group with a strong functional element superimposed on organic disease, and a fourth group of malingering cases. Warnings are given as to the dangers of manipulative attempts to reduce long-standing dislocations without the aid of open surgery, and in the miscellaneous type are included adhesions involving muscle, fascia, and so forth.

In the chapter on "The Prevention of Adhesions" the author reports his earlier work and the work of Willems demonstrating that even in acute and subacute cases intelligent and gentle movements, either voluntary or manipulative, may aid in the absorption of adhesions forming exudates, and may provide better drainage after surgery. The role of movement in chronic rheumatic diseases and in the prevention of deformity in fractures is discussed.

The diagnosis of adhesions is based on limitation of movement, pain, weakness, tenderness, recurring effusions and x-ray examination. The danger of any manipulation of a tuberculous joint is properly stressed.

In Chapter VI the general principles underlying the art of manipulation are discussed. "The use of extreme force is never necessary," both because of danger to surrounding structures and because the tearing of these adhesions usually leads to a reactionary subsequent joint stiffness. Merely putting a joint through its normal ranges of movement is not sufficient, a twisting movement by the operator is usually required, varying in nature in the different joints. Complete relaxation of the patient is necessary, and anesthesia often advisable. Aftertreatment, both physical and psychological, is of great importance, the latter especially with functional patients. In this chapter there is a discussion of the pros and cons of treatment of chronic arthritis by manipulation.

The succeeding chapters discuss the lesions of the lower extremities, the upper extremities, the spine and the sacroileal joints for which manipulative treatment is often advisable with the strong hope of betterment or cure. The methods appropriate to the different lesions and the different joints are described and illustrated. The

book concludes with two chapters, "The Dangers of Manipulation in Unsuitable Cases" and further details as to aftertreatment. As Fisher says, "The cure or alleviation of various disabilities by manipulation depends upon a delicacy and sensitiveness of touch which is to a certain extent 'inborn'." These gifts are often inherited, but it is a serious error to assume that unqualified practitioners have any monopoly of the necessary gifts."

The reviewer is of the opinion that the average American surgeon dealing with patients presenting lesions of the bones and joints employs manipulative methods of therapy less frequently and less successfully than the average British surgeon dealing with similar lesions. It is quite likely that we may sit at the feet of Hippocrates, John Hunter, Sir James Paget, Lucas Championnière and Sir Robert Jones and learn wisdom. We may even separate the grain from the chaff as Wharton Hood did from the successful bonesetter, Hutton. The reviewer recommends the book.

The Physiology and Pharmacology of the Pituitary Body
H. B. Van Dyke. Vol. 2. 402 pp. Chicago: The University of Chicago Press, 1939. \$4.50.

This book, the second of a series, is a careful and reliable review of the work of 1935-1938 in the somewhat confused field relating to the pituitary body. The author presents the essential clinical and experimental data of articles "flowing at the rate of approximately 750 yearly" and finishes each chapter with a summary of the reasonably proved facts. While the scope is largely physiological, to the clinician the summaries should be very welcome and pleasant reading and the main text should at least be useful for reference. The book gives an excellent epitome of recent work for the more academic reader and has the advantage of including the criticism of an expert.

The Synovial Membrane and the Synovial Fluid With special reference to arthritis and injuries of the joints
David H. Kling. 299 pp. Los Angeles: Medical Press, 1938. \$5.00.

The author has made a very thorough study of the synovial membrane and synovial fluid. He is also familiar with whatever other work has been done in this subject, and one of the interesting factors in his presentation is his constant mixing of his own work in observation with the work of others along the same line. The bibliography is complete and is well used in the text itself.

The laboratory study of the synovial fluid is of increasing importance in the study of arthritis and injuries to joints. This book gives an important place to practical considerations of laboratory methods. It is well written, concise and complete.

Health Officers' Manual: General information regarding the administrative and technical problems of the health officer
J. C. Geiger. 148 pp. Philadelphia and London: W. B. Saunders Co., 1939. \$1.50.

This small book is an attempt to outline municipal administrative procedures in public health. Its appeal is naturally limited. Of particular interest are graphic charts of the epidemiology of brucellar infections, plague, leptospirosis, relapsing fever, rickettsial infections and psittacosis, and two charts depicting the oral signs and symptoms of some fifty diseases. Aside from these, there is little of interest for the general practitioner of medicine.

The municipal health officer, however, can obtain advice on various administrative procedures which should be extremely helpful.

The New England Journal of Medicine

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VOLUME 221

OCTOBER 12, 1939

NUMBER 15

THE UNITED STATES MARINE HOSPITAL, PORT OF BOSTON

Massachusetts's Oldest Hospital

JOHN W. TRASK, M.D.*

CHELSEA, MASSACHUSETTS

THE origin and history of the Marine Hospital at the Port of Boston are closely associated with the growth of shipping and the development of medicine and medical institutions in New England. The Marine Hospital, originally located in Charlestown in 1804, and for the last one hundred and twelve years in Chelsea, is a product of Massachusetts. Of the eleven medical men who were at the head of the hospital during the first seventy-five years of its history, all were born in New England, eight in Massachusetts, two in New Hampshire, and one in Rhode Island. Nine had the degree of Doctor of Medicine (three of them honorary) from Harvard Medical School and seven were graduates of Harvard College.

The hospital owes its origin to the Boston Marine Society,[†] which at a meeting held at the Bunch of Grapes Tavern, Boston, on October 12, 1790 voted. That a Committee be appointed to consider what spot of ground may be the most convenient for the erecting a Marine Hospital, the kind of building that will be most convenient & its expense, also to make a Calculation of the annual income that will arise from a small Tax on seamen for the support of said Hospital & report at the next meeting. ‡ The committee was appointed and the members were recorded in the minutes as "Cap Mackay, Mr Russell, Dr Dexter Cap Deblais, Mr Tudor, Mr Hodgdon, Dr Scollay

The Dr Dexter on the committee was Aaron Dexter, professor of chemistry and materia medica at the Harvard Medical School, who had been elected to honorary membership in the Marine Society May 2, 1786.¹ John Adams, later president of the United States, was also a member of the society, having been admitted to membership March 3, 1769.²

At the next meeting of the society held three weeks later the committee reported that they were of the opinion "that some spot of the Heights of Charlestown, East of the Town is the most eligible situation for a marine hospital. The society further instructed the committee "to draw a petition to Congress, setting forth the utility of a

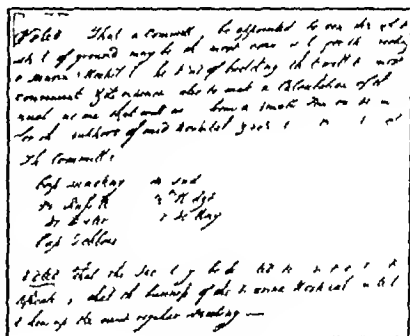


FIGURE 1

The part of the minutes of the meeting of the Boston Marine Society held at the Bunch of Grapes Tavern in Boston October 12 1790 showing the first action taken by the society with regard to the building of a marine hospital

Marine Hospital & pointing out the means of supporting one."

The minutes show that at a meeting of the society on January 4, 1791, the committee on the subject of the marine hospital reported a petition to Congress and sundry letters, which were accepted and vote ordered to be sent forward."

The annals of the Second Congress show that a bill had been introduced into the House of Representatives for the relief of sick and infirm seamen.³ In the first session of the next congress a committee was appointed to prepare and bring

*Medical officer in charge United States Marine Hospital, Port of Boston (Chelsea); medical director United States Public Health Service.

[†]A society incorporated 1754 having marine members and honorary members. Persons who are or have been in care of vessels are eligible to membership as sailing members. Others are eligible to honorary membership. Headquarters, 85 Broad Street Boston.

²From the original minutes of the meetings of the Boston Marine Society as kept at the headquarters of the Society.

in a bill for the relief of sick and disabled seamen," and Benjamin Goodhue, congressman from Massachusetts, was made chairman of the committee.

Finally after being repeatedly rewritten and amended the bill passed the House of Representatives April 12, 1798,⁵ and the next day was sent to the Senate, where it was referred to a committee consisting of Messrs Goodhue, Langdon and

fund in the treatment of sick and injured seamen all came under the Secretary of the Treasury, as the marine hospitals did up to July 1, 1939, when they were transferred from the Treasury Department to the Federal Security Agency.

When the act was passed, there was no general hospital in or near Boston,⁶ and no public hospital¹⁰ except those provided for the isolation and care of persons affected with contagious diseases

Boston, June 14, 1799

To
 Sir
 I have the honor to receive of your office a copy of the instructions from the Secretary of the Treasury to you to apply to me to attend the sick and wounded in the Marine Hospital in the Town of Boston. I agree with you to attend such sick and wounded in the Marine Hospital in the Town of Boston, and will within three weeks settle the terms of compensation, but for the present would only say that with you I agree that Castle William is the most suitable spot for a temporary hospital and that I am entirely agreed on a host and in labor for that purpose and to carry to effect this object it will be necessary to repair a barracks now in use on the fort place, for which it will be necessary to employ two or more carpenters one or more masons and laborers such materials as are now in the spot one or more other buildings will be wanted after the building is repaired. In the mean time it will be necessary to provide suitable persons for a steward and Nurse body of men and attendants and as I have been often a letter from the Secretary of the Treasury in answer to the letter upon the subject that should be done on the castle be found a suitable person. Therefore he would give orders to Major General Hamilton I suggest whether it would not be expedient that the Secretary of the Treasury should make to him the representation in person the order I will furnish you upon as it will be necessary with a detailed list of such articles as will be wanted in the same while I am with great respect yours that
 THOMAS WELSH
 Physician Surgeon in Charge
 Collector of the Ports of Boston and Charlestown

FIGURE 2

Letter of Thomas Welsh to the Collector of Customs, Ports of Boston and Charlestown, dated June 14, 1799, stating his willingness to accept the appointment as physician to the Marine Hospital

Read⁶ The chairman of this committee was the same Benjamin Goodhue who had been chairman of the committee in charge of the bill in the House, and in the meantime had been elected to the Senate. The bill passed the Senate July 14 and on July 16, 1798, was signed by President John Adams.^{7, 8}

The act required the masters or owners of vessels to pay to the collectors of customs at the rate of twenty cents per month for each seaman employed, and permitted them to retain a similar amount out of the wages of the seamen. This money was to be used to provide for the temporary relief and maintenance of sick or injured seamen. The act became effective September 1, 1798, and was essentially a form of compulsory sickness and accident insurance administered by the government to provide medical care and hospitalization for seamen. The collection of the money, the custody of the Marine Hospital Fund, as it was designated, and the expenditure of the

THE TEMPORARY HOSPITAL

The first result of the act at the Port of Boston, besides the collection of the money from the masters of vessels, was the employment of Dr. Thomas Welsh to have charge of the medical and surgical care of seamen and the equipping and putting into operation of a hospital to which seamen could be sent. Barracks buildings at the army post at Castle Island (also called Castle William, now Fort Independence) were repaired and put into use as a temporary hospital.

Thomas Welsh seems to have been an unusually active and capable physician. He was a graduate of Harvard College and had an honorary degree of Doctor of Medicine from the Harvard Medical School.¹¹ He was one of the incorporators of the Massachusetts Medical Society,^{12, 13} and was its first treasurer, holding that office from 1782 to 1798, corresponding secretary from 1805 to 1815 and vice-president from 1815 to 1823. He was elected a consulting physician on the first staff of the

Massachusetts General Hospital,¹⁴ held numerous other appointments at different times and was a man of varied interests and activities. His letter (Fig 2) to the Collector of Customs stating his willingness to accept the appointment of physician to the Marine Hospital follows.

Boston June 14 1799

Sir

In consequence of your application to me pursuant to Instructions from the Secretary of the Treasury to you to apply to me to attend the Military and Marine Hospital in this Vicinity I agree with you to attend such Hospital and will within a reasonable time settle the terms of compensation but for the present would only say that with you I agree that Castle William is the most suitable Spot for a temporary Hospital and the Place mutually agreed on as best calculated for that purpose and to carry into effect this object it will be necessary to repair a Barrack now in use in the first place, for which it will be necessary to employ two or more carpenters one or more masons and to procure such materials as are not now on the Spot. One or more other Buildings will be wanted after this Building is repaired.

In the Meantime it will be necessary to provide a suitable person for a Steward and Nurse Beds Bedding and Utensils and as I have been assured in a letter from the Secretary of War in answer to a letter upon the Subject that should any Place on the Castle be found suitable for this Purpose he would give order to Major General Hamilton I suggest whether it would not be expedient that the Secretary of the Treasury should make to him the Representation and known the order I will furnish you as soon as it will be necessary with a schedule of such Articles as will be wanted in the meanwhile I am with great Respect your Obedt

St

THOMAS WELSH

Benjamin Lincoln Esq^r

Collector of the Ports of Boston & Charlestown

One of Dr Welsh's early acts was the preparation of regulations for the conduct of the hospital. The regulations he drafted were approved by the President, and the Collector of Customs at Boston was so advised by the Secretary of the Treasury in a letter dated March 11, 1800. The regulations provided for a steward whose duty it was to purchase and issue supplies and preserve order in the hospital. They also provided for a principal nurse, staff nurses and orderly men. It was the duty of the principal nurse to see that the wards, beds, utensils and patients' clothing were kept clean and in order. There was to be a staff nurse for each ten patients. Convalescent patients were to perform such services as the surgeon should direct. Gambling of all kinds was prohibited. Diet tables were prepared providing for full, half, low, milk and fever diets.

According to Christian,¹⁵ Thomas Welsh was the first physician appointed and the first to treat

seamen at any port under the act of Congress providing for the establishment of marine hospitals for the treatment of sick and injured seamen. He held the position of physician and surgeon to the Marine Hospital at the Port of Boston for over two years.

THE FIRST PERMANENT HOSPITAL

In 1802, Congress provided that \$15,000 of the Marine Hospital Fund should be devoted to the erection of a permanent hospital in Massachusetts. For this purpose the Treasury Department secured from the Navy Department five acres of the tract of land in Charlestown purchased a short time before for use as a navy yard. A two-story and basement, brick hospital building, one hundred feet long by forty feet wide, was erected. It was ready for occupancy by the end of 1803 and the Marine Hospital patients were moved into it in January, 1804.

Charles Jarvis, who succeeded Thomas Welsh as physician to the Marine Hospital, was one of the incorporators of the American Academy of Arts and Sciences in 1780 and also of the Massachusetts Medical Society in 1781. Viets¹⁶ says of him: Charles Jarvis, who had studied in England and France, was an ardent patriot. Before the war he had been in the legislature and served as orator in Faneuil Hall." Dr Jarvis died at the Marine Hospital of "lung fever," November 15, 1807.¹⁷

The next physician in charge of the hospital was Benjamin Waterhouse, professor of the theory and practice of physic at the Harvard Medical School who introduced into New England the use of Jenner's vaccine as a preventive of smallpox and with the personal co-operation of President Thomas Jefferson also introduced it into Virginia.¹⁸ He first vaccinated his own son who thus was the first person vaccinated in America. Waterhouse had studied in England, Scotland and Holland and Viets¹⁸ expresses the opinion that when he returned from his studies of medicine under John Fothergill in London and Cullen, Black and Monro in Edinburgh and from his work at the University of Leyden he was probably the best-educated physician who had ever come back after study abroad.

Four years before his appointment as physician to the Marine Hospital Waterhouse had written a letter to the Collector of Customs of the Port of Boston mentioning the need of having access to a hospital so that the students of the Harvard Medical School might have the opportunity of actually seeing the conditions described in their medical lectures, stressing the fact that lectures alone did not constitute adequate training.

ing He stated that the need of demonstrating conditions at the bedside was felt particularly in his own teaching of the theory and practice of physic, that there was no hospital available for the purpose and that their hope rested in the establishment of a marine hospital for seamen¹⁰

Waterhouse was appointed physician to the Marine Hospital in November, 1807, and immediately became active in improving the plant and

Dr Townsend studied medicine under Joseph Warren, and as regimental surgeon accompanied General Joseph Warren at the battle of Bunker Hill²⁰ He was with the Army under Washington at Valley Forge, and in 1781 was appointed surgeon general of the hospital department of the Army²¹ He was physician of the Marine Hospital for twenty years, during a part of which time he was assisted by his son, S D Townsend,

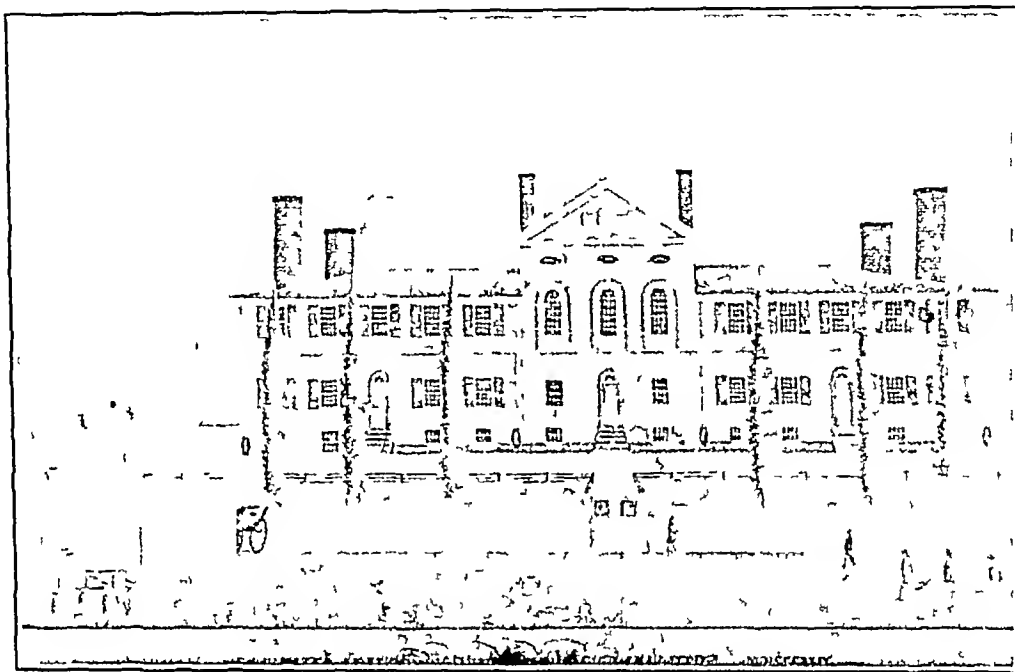


FIGURE 3

The first Marine Hospital building, erected in Charlestown in 1803 From a painting now at the Naval Academy at Annapolis Photographic copy furnished by courtesy of Rear Admiral Wilson Brown, superintendent of the Academy, who in sending it stated 'As the photograph shows, the paper is very old with the usual stain marks which our photographic staff did not think best to take out'

the service He saw the need for a building to serve as a barn and for storage purposes and had it built, and had trees and shrubs planted to beautify the grounds, planting one hundred quick-growing trees as a protection against the east winds, and acacia trees around the burying ground An outpatient service was begun for seamen who needed medical attention but did not require hospitalization An acre of ground was devoted to a hospital garden, more for the purpose of giving mild outdoor exercise to convalescent patients than for the produce raised Some of Waterhouse's medical pupils were kept constantly at the hospital Regular religious services by neighborhood clergymen were arranged Waterhouse served as physician of the Marine Hospital until 1809 when he was succeeded by David Townsend

who was later on the surgical staff of the Massachusetts General Hospital²² and consulting surgeon at the Boston City Hospital²³

During the war of 1812 Dr Townsend in the Marine Hospital took care of the sick and wounded from the frigate *Constitution* and of the prisoners from the *Guerrière* after their engagement, as well as the sick and wounded from other naval vessels and British prisoners from other engagements The officers and men of the Navy were beneficiaries of the marine hospitals from March, 1799, to February, 1811, when the Navy established its own fund and organized its own medical facilities However, the Navy sent its sick at the Port of Boston to the Marine Hospital up to the time it built its own hospital in Chelsea some years later

While in charge of the hospital, David Town-

send followed the policy of Benjamin Waterhouse and placed its clinical facilities at the disposal of the Harvard medical students.²⁴ He was elected a consulting physician on the first staff of the Massachusetts General Hospital.²⁵

THE SECOND HOSPITAL BUILDING

With the increase in shipping activities at Massachusetts ports and the greater number of sea

are there concentrated. Operations, various and important, are constantly occurring, and on this account, were economy entirely out of the question, we can strongly recommend students to avail themselves of its many privileges.

From 1841 to 1843 George Washington Otis was the physician in charge of the hospital. He was librarian of the Massachusetts Medical Society from 1838 to 1840 and recording secretary from 1840 to 1842.²⁶

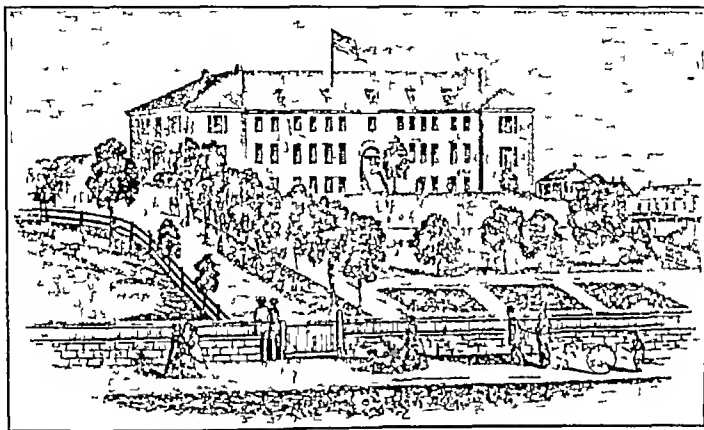


FIGURE 4

The second Marine Hospital building erected in Chelsea and occupied in 1827

men employed, a hospital with a greater bed capacity became necessary, and in 1826 a ten acre tract of land in Chelsea was purchased and a larger hospital constructed, to which the Marine Hospital patients were transferred 10 October 1827.

Dr Townsend remained in charge of the hospital up to the time of his death in 1829 when he was succeeded by Charles Harrison Stedman. While physician of the Marine Hospital, Dr Stedman revised and edited an American edition of Spurzheim's *The Anatomy of the Brain with a General View of the Nervous System*. This was published in 1834. It was during Dr Stedman's incumbency that there appeared in the *Boston Medical and Surgical Journal* for July 1836, an editorial entitled 'Marine Hospital' which criticized the Chelsea hospital as to architecture, construction and arrangement of the wards, but praised it as to location and outlook and ended with

During the next seven years the physician in charge was George Bailey Loring who, after leaving the Marine Hospital in 1850, was member of the Massachusetts House of Representatives, president of the State Senate, member of congress, United States Commissioner of Agriculture and United States Minister to Portugal.

After Dr Loring William Ingalls was at the head of the hospital. He was a member of the Massachusetts Medical Society, the Boston Obstetrical Society and the Boston Society for Medical Observation. In 1870 he was appointed to the surgical staff of the Boston City Hospital and in 1883 was put on its consulting board. He was also surgeon to the Children's Hospital. Harrington²⁷ says that Dr Ingalls was probably the first American surgeon to do a nephrolithotomy. He remained on duty at the hospital from 1850 to 1853 and was followed by Charles Augustine Davis.

Dr Davis was in charge for nine years to 1862, when he resigned to become surgeon to a Massachusetts volunteer regiment. There is an item in the *Boston Medical and Surgical Journal*

With all its defects, the Chelsea Hospital is an admirable school for gentlemen in the study of medicine and surgery. A multitude of diseases, from every clime,

for September 16, 1858, discussing a suit brought by W T G Morton against Dr Davis as physician-in-charge of the Marine Hospital for damages of \$5000 for having used ether as an anesthetic. It was presumably part of Morton's effort to be paid by the government for the use of ether. The suit appears to have been a friendly one, entered probably with Dr Davis's consent.

latter was in charge, Congress passed an act providing for the appointment of a "supervising surgeon" to supervise, under the direction of the Secretary of the Treasury, all the marine hospitals which had been established at the different ports.²⁸

Up to this time the physicians at the head of the Marine Hospital at the Port of Boston had been appointed from among the practicing physicians

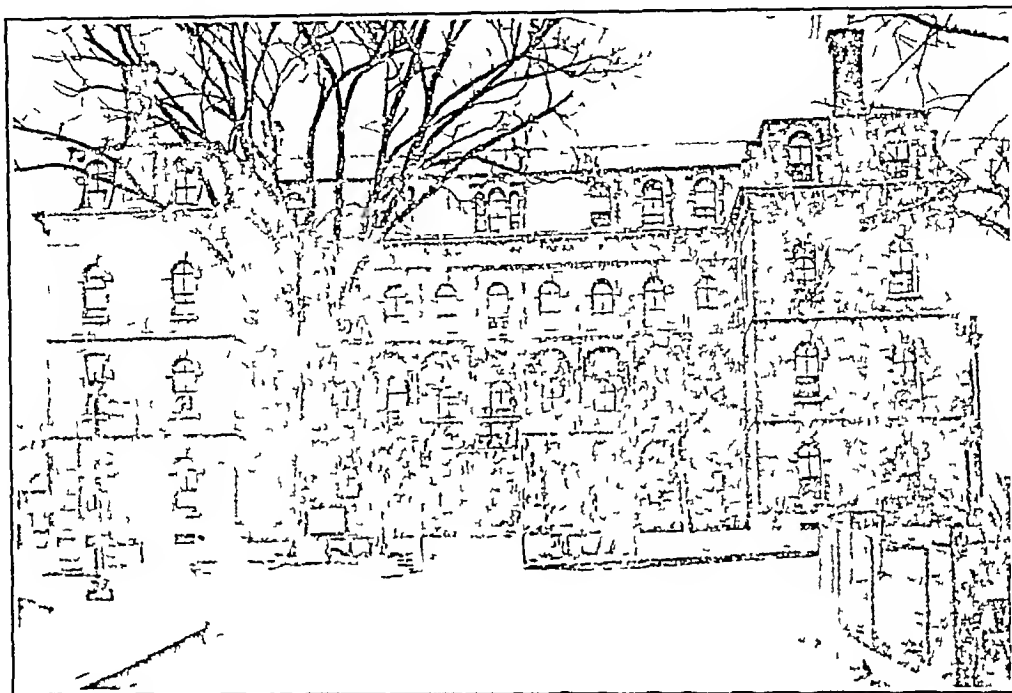


FIGURE 5

The third Marine Hospital building, the one now in use, erected in Chelsea in 1857. It originally had three stories, the fourth was added later.

THE THIRD HOSPITAL BUILDING

The shipping at Massachusetts ports continued to increase, and with it the number of seamen and the need for hospital beds. The requirements became greater than the capacity of the second hospital building could meet. A larger hospital was a necessity. As Chelsea found that the hospital grounds interfered with its desired street development, ten acres of the Naval Hospital reservation were secured as a site for a new and larger building, the third which had housed the Marine Hospital or the fourth if one counts the barracks at Castle Island used for the first or temporary hospital. It was while Dr Davis was in charge that the new building was constructed and the patients moved into it in 1860. This building is the one now in use. It is a four-story red brick structure located on a hill overlooking the inner harbor.

John Wheelock Graves of Lowell, Massachusetts, was in charge from 1862 to 1869, and Amos Bigelow Bancroft from 1869 to 1877. While the

of Boston and vicinity Dr Bancroft was the last physician so appointed. After 1873 appointments of medical officers were made, not to particular hospitals but to the general service, and after passing examinations in medical subjects. From this time on the medical officers seldom remained on duty at the hospital more than four years, being transferred periodically from one to another of the marine hospitals, of which there were seven in 1874.

Subsequent to 1878 Congress from time to time imposed additional duties on the Marine Hospital Service. These related to maritime quarantine, interstate quarantine, medical inspection of immigrants, research into the causes and prevention of diseases of man, supervision of the interstate sale of biological products through a system of licensing the manufacturing laboratories and numerous other matters relating to the public health. With these added functions the name "Marine Hospital Service" ceased to be suitably descriptive and was changed in 1902 by act of

Congress to the "United States Public Health and Marine Hospital Service. Congress continued to add to the public health functions of the service and the name, which was cumbersome, was changed to a shorter one, "United States Public Health Service," in 1912. However, the hospitals continued to be called marine hospitals, as they had been for the more than a hundred years of their existence.

The activities of the hospital at the Port of Boston increased steadily with the growth of the country. The number of patients treated

Federal Security Agency under the administration of Paul V McNutt.

To meet the needs of the slowly but ever increasing demands made on the hospital at the Port of Boston and because of the overtaxed condition of the present building, a new hospital is under construction in the Brighton district of Boston which will probably meet the needs for another eighty or more years, as the present building has done. This new building will be the fourth which has housed the hospital since its beginning not counting the buildings at Castle

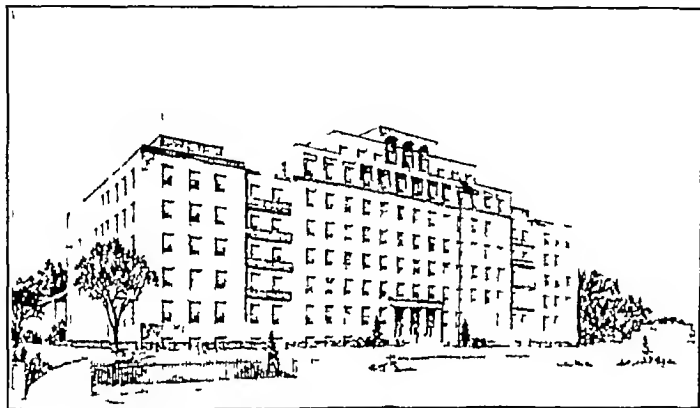


FIGURE 6.

The fourth Marine Hospital building now under construction on Warren Street near Commonwealth Avenue Boston (architect's sketch)

in the hospital in 1820 was 382, in 1832 it was 521 and in 1870 it was 795. The activities for the year ending June 30, 1938, were

Total number of patients treated	13,155
Number of patients treated in hospital	2,148
Number of hospital-patient days	59,942
Number of patients furnished outpatient treatment	11,007
Number of outpatient visits	48,891
Number of physical examinations	8,656

With the passage of time and the growth of the country's merchant marine, not only have the demands made on the marine hospitals become greater but their number as well has been increased, until today there are twenty six hospitals of which one is a tuberculosis sanatorium in New Mexico and one a leprosarium in Louisiana. All these were hospitals of the Treasury Department and were administered by the Secretary of the Treasury through Surgeon General Thomas Parran of the United States Public Health Service, up to July 1, 1939, when the Public Health Service Bureau was transferred to and made a part of the

Island which were used as a temporary hospital previous to 1804.

The collection of the twenty cents a month from seamen provided in the original act of July 16, 1798 after the first few years proved not to be adequate to maintain the marine hospitals, and the deficits were met annually by appropriations of Congress. In an effort to make the service self supporting forty cents per month was collected beginning August 1, 1870. However, the funds obtained by the increased assessment were in turn found insufficient. The result was that Congress by an act approved June 26, 1884 abolished the taxes on seamen and the marine hospitals were maintained for a time from the proceeds of the tonnage taxes. Beginning with the year 1907 the use of the tonnage tax was discontinued and the expenses of the marine hospitals were provided for by annual appropriations of Congress.

After the collection of money from seamen to maintain the marine hospitals was discontinued

the services of the marine hospitals were made available to certain government employees, as well as to the seamen, so that at the present time persons eligible for treatment at the marine hospitals are merchant seamen, officers and enlisted men of the United States Coast Guard, officers and seamen of vessels of the United States Coast and Geodetic Survey, Lighthouse Service and Bureau of Fisheries, and of certain other government vessels, certain keepers and assistant keepers of lighthouses, cadets on state school ships, federal government employees sustaining injuries while in the performance of duty, and lepers. The lepers are admitted to the leprosarium at Carville, Louisiana. Seamen from foreign vessels and certain beneficiaries of the federal government may also be admitted, but as pay patients.

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THE TREATMENT OF LEUKOPLAKIA BUCCALIS AND RELATED LESIONS WITH ESTROGENIC HORMONE*

IRA T NATHANSON, MD,† AND DAVID B WEISBERGER, MD‡

BOSTON

SEVERAL years ago it came to our attention as a result of independent observations that leukoplakia of the oral mucous membranes was not uncommonly associated with disturbances in the menstrual cycle and particularly with the menopause. Since similar lesions of the vulva, vagina and cervix occur in the same age group, it seemed possible that these analogous histologic abnormalities were associated with the same basic systemic factors, namely the well-established diminution in the production, or an alteration in the metabolism of the sex hormones which occurs in the later decades of life. A study of possible etiologic factors and modes of treatment of leukoplakia is especially significant since it not infrequently accompanies or is a precursor of carcinoma. The etiology has remained obscure, although many factors have been suggested which

may be sole or contributing causes. In 1934 a thorough study of possible etiologic agents and of clinical behavior of the disease and an extensive review of the literature were made by Sturgis and Lund¹ of this institution. Repetition of the information is therefore not included here. This paper presents observations on a selected group of patients with leukoplakia buccalis in our clinic and reports on the results of treatment with estrogenic hormone, based on the premise of a sex-hormonal deficiency. A detailed clinical, laboratory and histological study of these same patients will be reported later.

A total of 38 patients with leukoplakia buccalis, of whom 25 were women and 13 were men, is included in this report.

The leukoplakia and associated symptoms such as burning and dryness of the oral membranes were encountered in three groups of women: a young age group (4 cases), in which there was amenorrhea, which was secondary to or resulted from castration, a pre-menopausal group (4 cases), in which there were marked irregularities in the

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menstrual cycle, where previously the rhythm had been regular, and a menopausal group (17 cases), in which these lesions were frequently associated with typical vasomotor symptoms. The men with but few exceptions presented histories of sexual decline.

Routine observation of a large series of patients seen in the clinic with these lesions over a period of years frequently revealed a certain sequence of events. Many of these first entered the clinic complaining of burning or other abnormal sensation of the tongue and buccal mucosa. No definite lesions could be found, although the mucous membranes on occasion did not present the usual normal pink color. In the cases with an acute onset the mucosa appeared hyperemic in spots, or the entire membrane was involved. When symptoms were of relatively long standing the mucosa was pale. Most of this latter group of patients complained of dryness and stickiness. After the onset of these subjective symptoms the mucous membranes seemed to become edematous with a loss of translucence. A "milky film" was then seen to appear and usually covered the entire mucosa. Shortly thereafter the membrane became gray-pink, finely wrinkled and appeared much like a moistened cigarette paper. In some cases small red areas appeared where the epithelium was denuded. These areas sometimes became confluent and involved the entire mucosa. Following this, persistent ulceration was noted in some of the patients. In other cases the milky film became accentuated and presented a white membrane which was adherent to the underlying structure. This process was either patchy linear streaked or diffuse. The edges, although irregular, were fairly well defined. The process described we have designated as the cigarette-paper type. In some cases the process remained stationary at this stage, but frequently it became more diffuse and thicker until it presented as a typical papillary hyperkeratosis. (This is not to be confused with the "wart" lesions which appear only on the gingivae and palate from ill fitting dentures.) In several cases the lesions became lichenified and appeared much like the hide of an elephant. Carcinoma appeared eventually in some of the patients who were not included in the study but under observation.

The most commonly involved areas, arranged in order of frequency, were the mucous membrane of the cheek, particularly in the molar region, the tongue, the floor of the mouth and the palate. In some of the patients cycles of activity of the lesions were established. The periods of quiescence finally became shorter and the process persistent. Some of these lesions showed regres-

sion or remissions when preventive measures based on possible etiologic factors were instituted. The measures consisted of abstinence from smoking, removal of decayed teeth, changing or removal of ill fitting dentures, dental hygiene and the treatment of syphilis, when present. In many cases diets supplemented by vitamins were given, without any appreciable effect on the lesions. Local treatment such as desiccation, cautery, x-ray and radium sometimes produced satisfactory results. In spite of such treatment the mucosa was not restored to its normal appearance, for it retained fine lines of thickened membrane which were usually the site of future recurrences.

In the group here reported treatment directed toward sex hormonal deficiency was instituted only after other measures tried over relatively long periods had failed. It should be emphasized further that no treatment other than that with estrogens was used when the observation as to the effect of this therapy was made. This was obviously necessary since the use of any other measure would have given rise to too many variables. The effect of the administration of androgenic preparations will be reported in a later publication.

The estrogens* were administered in two forms, estradiol benzoate, which was used parenterally and alpha estradiol which was given orally. In one group the usual dose for estradiol benzoate was 10,000 RU (rat units) in 1 cc. of sesame oil given every other day for six injections (total dose 60,000 RU). This was supplemented by the oral administration of tablets of alpha estradiol for a total daily dose of 0.17 to 1.00 mg. given over the same period. In the other group treatment consisted of oral medication only, the usual daily dose varying from 0.17 to 0.50 mg. alpha estradiol per day given over a period of ninety to one hundred and twenty days. In some cases equivalent doses of alpha estradiol dissolved in 95 per cent alcohol were given. This has advantages over the tablet form in that the dose can be more easily regulated and that absorption probably takes place more readily in the gastrointestinal tract. Except in those patients who had not responded to therapy the medication was not given for any longer periods of time.

RESULTS

The results of treatment as well as other pertinent data are given in Table 1. Complete disappearance of the lesions occurred in 16 (42 per cent) of the 38 patients, marked improvement in

* We are indebted Drs. Gregory Strassell and M. J. Gilbert of the Schering Corporation, Kenilworth, New Jersey and to Dr. R. D. Slusher of Hoffmann-La Roche Incorporated, Nutley, New Jersey for generous quantities of estradiol supplied under the trade names of Progeston and Menformon, respectively.

TABLE 1 *Summary of Cases*

PATIENT	AGE AND SEX	STATE OF MENSES	DURATION OF SYMPTOMS	SUBJECTIVE SYMPTOMS	OBJECTIVE SYMPTOMS	PREVIOUS TREATMENT	TOTAL PARENTERAL THERAPY	DAILY ORAL THERAPY	DURATION OF TREATMENT	RESULT
			<i>mo</i>				<i>r u</i>	<i>mg</i>	<i>days</i>	
B R	51 F	Irregular	18	Burning soreness	Ulceration hyperemia	0	60 000	0 50	21	Improved
A D	49 F	Artificial menopause	6	Dryness burning	Superficial leukoplakia (cigarette paper type) ulceration	0	60 000	0 50	21	Lesion disappeared
M F	42 F	Irregular	7	Dryness burning	Superficial leukoplakia (cigarette paper type) hyperemia	0	60 000	0 50	21	Lesion disappeared
S T	35 F	Artificial menopause	12	Burning	Superficial leukoplakia (cigarette paper type) hyperemia	Removal of fillings	60 000	0 50	21	Lesion disappeared
A L	48 F	Spontaneous menopause	6	Dryness burning	Superficial leukoplakia (cigarette paper type), ulceration	0	60 000	0 50	21	Lesion disappeared
M B	47 F	Spontaneous menopause	13	Soreness	Ulceration hyperemia	0	60 000	0 50	21	Improved
N C	51 F	Spontaneous menopause	36	Burning	Superficial leukoplakia (cigarette paper type), hyperemia	0	60 000	0 50	21	Improved
R H	44 F	Spontaneous menopause	8	Burning	Superficial leukoplakia (cigarette paper type) hyperemia	Vitamins, removal of fillings	60 000	0 50	21	Improved
H F	32 F	Amenorrhea	7	Burning dryness	Superficial leukoplakia (cigarette paper type)	Vitamins	60 000	0 50	21	Lesion disappeared
A G	43 F	Irregular	6	Soreness burning	Superficial leukoplakia (cigarette paper type) hyperemia	Removal of dentures	60 000	0 50	21	Improved
L B	34 F	Artificial menopause	10	Burning	Superficial leukoplakia (cigarette paper type), hyperemia	Vitamins	60 000	0 50	21	Lesion disappeared
A R	36 F	Artificial menopause	3	Burning	Superficial leukoplakia (cigarette paper type) hyperemia	Vitamins	60 000	0 50	21	Improved
J J	41 F	Irregular	12	Dryness burning	Superficial leukoplakia (cigarette paper type) hyperemia	Removal of dentures	60 000	0 50	21	Lesion disappeared
R M	48 F	Spontaneous menopause	6	Dryness burning	Superficial leukoplakia (cigarette paper type) ulceration	Removal of dentures	60 000	0 50	21	Lesion disappeared
A D	50 F	Spontaneous menopause	36	Dryness burning	Hyperemia	Removal of dentures	60 000	0 50	21	Lesion disappeared
M R	48 F	Spontaneous menopause	6	Burning	Superficial leukoplakia (cigarette paper type) hyperemia	Removal of dentures	60 000	0 50	21	Lesion disappeared
A P	48 F	Spontaneous menopause	11	Burning dryness	Superficial leukoplakia (cigarette paper type) hyperemia	Removal of dentures	60 000	0 50	21	Improved
E. C.	18 F	Amenorrhea	12	Dryness	Milky film	Vitamins	60 000	0 50	21	No change
H A	50 F	Spontaneous menopause	36	Burning dryness	Thick leukoplakia, ulceration	Vitamins	60 000	0 50	21	Improved
D B	45 F	Spontaneous menopause	120	Burning dryness	Papillary leukoplakia	Desiccation removal of dentures vitamins	200 000	1 00	90	Improved
E. F	55 F	Spontaneous menopause	60	Soreness burning	Superficial leukoplakia (cigarette paper type) ulceration hyperemia	Removal of dentures vitamins	0	1 00	120	Improved
N C	72 F	Spontaneous menopause	12	Burning	Superficial leukoplakia (cigarette paper type)	0	0	0 50	90	Lesion disappeared
E S	65 F	Spontaneous menopause	6	Soreness dryness	Papillary leukoplakia	0	0	0 33	60	Improved
E. M	68 F	Spontaneous menopause	6	Dryness	Superficial leukoplakia (cigarette paper type)	Removal of dentures	25 000	1 00	30	No change
M H	67 F	Spontaneous menopause	24	Soreness burning	Thick leukoplakia	Desiccation removal of dentures	0	1 00	120	No change
R W	59 M	—	18	Soreness	Superficial leukoplakia (cigarette paper type)	Radium	0	0 50	120	Lesion disappeared
C. M	69 M	—	6	Soreness, burning	Papillary leukoplakia ulceration	Removal of dentures	0	0 50	90	Improved
J C.	49 M	—	3	0	Superficial leukoplakia (cigarette paper type)	0	0	0 50	60	Lesion disappeared

TABLE 1 *Summary of Cases (Concluded.)*

PATIENT	AGE AND SEX	STATE OF MUCOSA	DURATION OF SYMPTOMS MO	SUBJECTIVE SYMPTOMS	OBJECTIVE SYMPTOMS	PREVIOUS TREATMENT	TOTAL PAIN TO ALL THERAPY r. m.	DAILY ORAL THERAPY mg	DURATION OF TREATMENT day	RESULT
J. H.	88 M	—	36	0	Papillary leukoplakia	X-ray removal of dentures	0	0.50	120	No change
M. T.	66 M	—	96	0	Superficial leukoplakia (cigarette-paper type)	Removal of dentures, desiccation	0	0.50	90	Improved
E. P.	62 M	—	24	Burning	Superficial leukoplakia (cigarette-paper type)	Smoking discontinued	0	0.50	90	Lesion disappeared, mastitis
L. L.	54 M	—	10	0	Papillary leukoplakia	Smoking discontinued	0	0.50	60	Lesion disappeared
T. D.	60 M	—	10	Burning, dryness	Papillary leukoplakia	Smoking discontinued	0	0.17	90	Improved
A. C.	76 M	—	60	0	Papillary leukoplakia	Removal of dentures, desiccation	0	0.50	120	No change
A. C.	53 M	—	18	Burning	Superficial leukoplakia (cigarette paper type)	Smoking discontinued	0	0.1	60	Lesion disappeared, mastitis
H. W.	52 M	—	36	Burning	Thick leukoplakia	Desiccation	0	0.50	90	Improved
E. S.	40 M	—	96	Burning	Papillary leukoplakia	Removal of dentures	0	0.50	150	No change
L. F.	68 M	—	4	Burning, dryness	Superficial leukoplakia (cigarette-paper type) ulceration	0	0	0.50	60	No change

15 (39 per cent), and no change in 7 (19 per cent).

The first change noted in the mucosa after the onset of treatment was edema and haziness. The change is much the same as that described when the lesions are developing. It often appeared in about a week when the hormone was administered parenterally, and in four to six weeks when it was given orally. In some cases hyperemia became evident but as a rule the mucosa tended to assume a healthy pink appearance. During the course of treatment the leukoplakic membrane could occasionally be detached with ease from the underlying mucosa leaving a pink, smooth surface. When the treatment was effective the lesions shrunk gradually and eventually disappeared altogether or were replaced by fine linear streaks which were barely discernible (Figs 1 and 2). The process of healing seemed to proceed in a retrograde fashion through those changes which we had observed in the development of the lesions.

In the majority of the cases in which treatment was successful there was usually a reappearance of the leukoplakia in three to six months after the therapy was discontinued. This suggested that a maintenance dose was necessary in order to prevent recurrence once the lesion had regressed. It was found therefore, that 0.17 mg of alpha estradiol given daily by mouth was usually sufficient to keep recurrences at a minimum.

It can be seen that those patients who responded successfully to therapy were in large part those in whom the lesions were of relatively short duration (under two years) and not too far advanced.

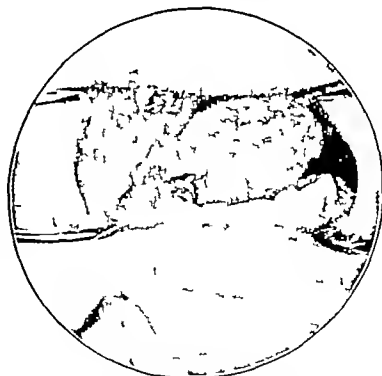


FIGURE 1 *Leukoplakia of Oral Mucous Membrane before Treatment*

We continued treatment on those who had not responded, with the hope that the same effect might be produced with more vigorous therapy.

DISCUSSION

From the results given above it seems possible that an alteration in metabolism of the sex hor-

mones may be an etiologic factor in many patients with leukoplakia buccalis and similar lesions. The fact that the symptoms and lesions reappeared after discontinuation of this type of treatment fortifies this view. Single assays of the urinary excretion of the estrogenic and androgenic hormones² on 4 patients who were not obviously deficient revealed values considerably below normal.

Several reports have appeared on the successful treatment of leukoplakia of the vulva and vagina,

alteration in the metabolism of the sex hormones should not be taken to mean that this is the sole or exciting factor. We believe, however, that it is an important and possibly a fundamental one. In other words, a similar state of the membranes may exist in all persons who have undergone sex-hormonal decline or failure. Hence it is conceivable that other factors, particularly those described by Sturgis and Lund,¹ acting on a substrate produced by the hormonal deficiency, may give rise to the lesions described.

COMPLICATIONS OF TREATMENT

In two men typical mastitis developed after three months of treatment by the oral route. The lesions regressed when treatment was discontinued. Since there are many reports of the development of mammary carcinoma in mice after the administration of estrogen, and since it is commonly accepted that leukoplakia is frequently a precursor of malignant disease, we believe that treatment should be carefully supervised and should not be given over too long a period of time in too large a dosage.

CONCLUSIONS

Evidence is presented which suggests that leukoplakia buccalis and similar lesions are associated with alterations in the menstrual cycle in women, and with a deficiency or disturbed metabolism of the sex hormones in both sexes. Treatment with estrogen based on this evidence has resulted in the complete disappearance of the lesions in 42 per cent, marked improvement in 39 per cent and no improvement in the remaining 19 per cent of 38 patients. In general the women responded more satisfactorily to the treatment than did the men. Although further observation is needed, it is suggested that this type of therapy in combination with other well-recognized procedures may prove of value in the treatment of leukoplakia buccalis.

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FIGURE 2 *Leukoplakia of Oral Mucous Membrane after Treatment*

Note the linear streaks which remained

as well as of kraurosis vulvae and accompanying symptoms, by the use of the estrogenic hormone.³ It is also interesting that Mortimer et al.⁴ have obtained relief in patients with atrophic rhinitis by the use of these same hormones. Many of our own patients had atrophic, pale, nasal mucous membranes, and in some cases a chronic rhinitis, associated with the leukoplakia. These observations lend further support to the thesis that these changes occur in the presence of a sex-hormonal deficiency which is generalized in its effect.

The suggestion that there is a deficiency or

THE RECIPROCAL PHARMACOLOGIC EFFECTS OF AMPHETAMINE (BENZEDRINE) SULFATE AND THE BARBITURATES*

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ON FIRST examination the effects of the barbiturates and of amphetamine (Benzedrine) sulfate would seem to be fundamentally opposite and therefore irreconcilable. The barbiturates are sedatives and in large doses anesthetics and narcotics. They tend to lower the metabolic rate, in large doses they lower the blood pressure, in extreme doses they create ataxia, nystagmus, abolition of the abdominal reflexes, torpor, depression and even mental confusion and delirium. In general they retard the mental processes and produce sleep.

That very interesting drug, amphetamine sulfate, better known to the profession as Benzedrine Sulfate, in general seems to work in the opposite direction on the organism. It has remarkable sleep-disturbing qualities, and in fact this effect of the drug is obtainable with smaller doses and lasts a longer time than do the purely visceral responses. This capacity to disturb sleep or to produce wakefulness is the basis of its great value in the peculiar sleeping disease called narcolepsy.¹ In most individuals small doses bring a sort of exhilaration, although in certain individuals and in large doses the effect is a certain nervousness or hyperexcitability which is unpleasant.²

Like all drugs of adrenergic type notably adrenalin and ephedrine, together with the newer preparations called Propadrine, Neosynephrin and Paredrine, amphetamine sulfate elevates the blood pressure, and tends to constrict the caliber of the blood vessels, acting as a vasoconstrictor, whether by central or peripheral mechanisms or both and to relax smooth muscle elsewhere. Thus it relaxes spasms of the gastrointestinal tract, in this manner acting as an aid to x-ray studies; it is therefore useful to a certain extent in the milder cases of spastic states of the gastrointestinal tract. It relaxes the genitourinary tract and has a field of usefulness which deserves exploration. It dilates the pupil, and because of its shortness of action is being used in combination with homatropine to produce mydriasis useful to the ophthalmologist.³

It is a synergist to atropine in all the physio-

logic effects of that drug,⁴ or, conversely, atropine is a synergist to amphetamine sulfate because it blocks or inhibits the action of the parasympathetic effects of amphetamine sulfate and allows the sympathetic effects to be more firmly established. This combination with atropine is one of the more dangerous uses of the drug.

While the opposing effects of the barbiturates and amphetamine sulfate are quite clear-cut, they may nevertheless be used to produce very worth while and reciprocal pharmacologic clinical effects. This paper is presented for the purpose of pointing out that where the barbiturate or sedative effect is desirable, the narcotic and ataxic effect can be lessened or completely antagonized by the judicious use of small doses of amphetamine sulfate. On the other hand where the amphetamine effect is desirable and the excessive reaction in the direction of disturbing sleep and producing hyperexcitability makes its proper clinical use difficult or impossible, the judicious use of small doses of the barbiturates is of great value.

Thus when the barbiturate effect is desired, large doses may be used and the undesirable effects counteracted in part or in whole by small doses of amphetamine sulfate. When large doses of the latter are desirable, the disadvantageous and disturbing reactions may be obviated and relieved by small doses of the barbiturates.

CLINICAL SITUATIONS IN WHICH THE COMBINED AND CORRECTIVE USE OF THE DRUGS IS VALUABLE

In a prolonged and continuing research on epilepsy we⁵ have shown that in the chronic epileptic with many seizures, large doses of phenobarbital are of value. When such doses are used and in a time relation to the seizures, that is to say where the drugs are administered at a time of the day when seizures are expected there is a very marked reduction of epileptic attacks. In some individuals 3 to 6 gr. of phenobarbital a day is required. As a result of such large doses some patients become stupid and often ataxic, presenting the classical picture of barbiturate poisoning. In such cases the judicious use of amphetamine sulfate, from 10 to 20 mg. a day, restores the patient to a more nearly normal mental and neurologic condition and he can then receive large doses of phenobarbital with

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†This study was aided by grants from the Commonwealth of Massachusetts and the Rockefeller Foundation.

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out ill effects. Amphetamine sulfate in itself, as has been shown by the work of Merritt and Putnam,⁶ has no effect on convulsions, either to increase or to decrease them.

The following case histories are typical.

CASE 1 A 55 year-old lawyer had his first attack of epilepsy at 50 years of age. A complete neurological examination, including lumbar puncture, x-ray, air injection and so forth, revealed no organic basis for his attacks. With a dose of $1\frac{1}{2}$ to 2 gr of phenobarbital a day, no relief was obtained. When the dose was increased to 3 and 4 gr a day the attacks ceased, but the patient found himself in a plight in which the cure was about as bad as or worse than the disease, since his speech became rather thick, his mind dull, and, while he did not have ataxia, his general capacity to move and think co-ordinately and rapidly was definitely impaired. This patient was started on one tablet (10 mg) of amphetamine sulfate in the morning and one half tablet (5 mg) at noon. In a very short time the torpor disappeared, the depressed mood vanished, and he was able to carry on his work perfectly well.

CASE 2 A 40 year-old man, a chronic epileptic, having as many as one hundred seizures a year of major type on a dose of $1\frac{1}{2}$ gr of phenobarbital, had his attacks reduced to thirty a year, of lesser severity, with a dose of 4 gr of phenobarbital a day. This, however, brought a certain amount of torpor, slowness of thought and general slowness of motion. Small doses of amphetamine sulfate adjusted to his needs brought about relief from the phenobarbital poisoning, yet maintained the good effects of the inhibition of epileptic attacks by phenobarbital.

These two cases are examples of many which have been under treatment at the Grafton State Hospital and in private practice.

INSOMNIA AND KINDRED DISTURBANCES

In many of the neuroses, a reversal of the cycle of energy and wakefulness is observed.⁷ The sleep-rest-recuperative process is disturbed, so that individuals suffer from insomnia of one type or another at night and are restless and incapable of relaxation during the day, even though they feel drowsy and completely worn out. The obvious indication in these cases is sedation, especially at night, and also during the day in order to produce a more equable state. The use of sedatives of the barbiturate series is strongly indicated, but in many cases there is a hangover of narcosis if sufficient doses of barbiturate are given. The result is that while sleep is obtained, the relief is offset by the very disagreeable after-effects and the persistence of the torpor into the day.

It has been my practice for the last three years to give such patients from 5 to 15 mg of amphetamine during the day in divided doses thus starting the waking mechanism. There is, I am convinced, a physicochemical apparatus by which the individual is put to sleep at night and another by which he is awakened and his mechanisms set

into motion, by what is here called the waking process. Both these functions are impaired in many of the neuroses.

The judicious use of the barbiturates or other sedatives toward night and of amphetamine sulfate aided by small doses of caffeine or strychnine in the morning re-establishes a normal cycle in many cases, and thus offers opportunity for such other constructive efforts as are necessary for any individual suffering from a neurosis.

AMYTAL AND AMPHETAMINE SULFATE

Of special interest is the relation between Amytal and amphetamine sulfate. We⁸ have shown that the narcotic effects of Amytal can be offset by amphetamine sulfate. Thus if a narcotic dose of intravenous Sodium Amytal is established for any individual, the introduction of from 20 to 30 mg of amphetamine sulfate intravenously given at the same rate as the Sodium Amytal will prevent the narcosis. The patient remains awake, although he may be somewhat drowsy for a short time.

An interesting side-result, which I have utilized in the treatment of depressions, becomes manifest by these experiments. The patient becomes talkative and often quite exhilarated. In many cases where there is profound depression the individual feels normal for a short time, his depression disappears and for this period he acts as if it had been cured. Unfortunately this condition does not last, but the indications were so pertinent that a series of experiments was started at the McLean Hospital in conjunction with Dr. Kenneth J. Tillotson and in private practice, whereby patients receive as much as 3 gr of Sodium Amytal by mouth and 5 to 10 mg of amphetamine sulfate two or three times a day, with a resultant marked change in mood and an incomplete approximation to normal feeling and activity. The combined drugs do not cure the depression, but they keep the patient comfortable while Nature is bringing about the cure. Whether or not the attacks are shortened is a question which we are studying. It may be stated, however, that no combination of drugs used, with the possible exception of Metrazol, has anything like the value of either Sodium Amytal or Amytal in combination with amphetamine sulfate in the treatment of depression.

Moreover, in psychiatric practice, in the case of shut-in individuals who will not communicate their ideas, Amytal and amphetamine given in this way, or with the former given first to the point of narcosis and the latter then used to wake the patient up, produce a loquacity which is of value from the standpoint of diagnosis and

which might well be of value in criminologic situations. At any rate, abundant clinical material confirms this statement.

CASE 3 A 45-year-old woman, who passed through a marked depression when she was 20 years of age which lasted 2 years gradually developed a marked depression with anxiety unreality obsessive ideas and agitation at the age of 42. She was sent to an institution from which she was removed in 1937 a year ago she was first seen for personal care. Six grains of Sodium Amytal injected intravenously with 30 mg of amphetamine sulfate injected subcutaneously produced an effect which she described as a feeling of entire normality and happiness for several hours, after which she lapsed into her former depression. She was then given 3 gr of Sodium Amytal and 10 mg. of amphetamine sulfate by mouth twice a day with the result that she returned to her duties as wife, mother and housekeeper. While she was still depressed, her general condition had greatly improved so that what had been a disabling psychosis was greatly ameliorated.

It is to be emphasized that many patients with depression do not improve to any marked extent under this treatment. A sufficient number do however, to make it worthy of a trial in any case.

AMPHETAMINE SULFATE EFFECT MITIGATED BY BARBITURATES

A case in which a combination of amphetamine sulfate and one of the barbiturates, Mebaral (*n*-methylethylphenyl barbituric acid) was used, is summarized as follows:

CASE 4 A 23-year-old man received an injury to his spinal cord which produced a complete paralysis of the legs and a cord bladder and bowel. The use of his legs returned. The bladder condition became very troublesome, since he was unable to go anywhere because of the constant dribbling of urine, which became increased by any exertion or jouncing of the body. Examination showed a markedly spastic urinary bladder contracted to one fourth its usual size. Since in a previous paper we⁹ had shown that amphetamine sulfate dilates the genitourinary tract, especially the bladder this drug was administered in a dose of 20 mg. a day and under this regime the bladder dilated so that the individual was able to hold a larger amount of urine. However he reported that he was unable to sleep well as a result. He further stated that he had been able to have sexual intercourse since the administration of the drug but that the orgasm was almost instantaneous. He was put on Mebaral 3 gr twice a day as a result of which his sleep improved. He was able to maintain the improved bladder condition and, curiously enough, his orgasm was delayed sufficiently for fairly normal sexual relations.

In cases where amphetamine sulfate is used for weight reduction,¹⁰ especially in the definitely neurotic and excitable patient to whom eating is a sort of relief from boredom and depression its use alone is often attended by an increase of the excitability to the point where the administration of the drug becomes difficult or impossible. In such cases the addition of 1/4 or 1/3 gr of phenobarbital or of small doses of other seda-

tives, including bromides, to each 10 mg of amphetamine sulfate operates well, in that the appetite reduction is maintained and a more equable mood established, so that the patient finds it easier to follow directions as to dieting.

It is to be emphasized that in all weight reduction, dieting is the main, and practically speaking except for the pathologic cases the only imperative factor involved. The ability of the patient to follow directions or his willingness, or both, have to be reinforced. The physician operates in these cases by his personal influence and, I believe, by the judicious use of drugs to enhance the capacity of the patient to diet.

SUMMARY

In the conditions discussed above, the main effect of the pharmacologic means used is ameliorative and not directly or immediately curative. In other words, the drugs used are not specifics. They help, I believe, in re-establishing an approximation to normal conditions, and consequently the latent forces of the organism for cure or remission are enhanced.

The barbiturates have highly important sedative effects. Amphetamine (Benzedrine) sulfate has important stimulating effects. These effects do not necessarily oppose one another, and the drugs can be used to produce mutually corrective results which are of great value.

Needless to say, as with all pharmacologic agents, permission to use them should be confined entirely to physicians. Neither the barbiturates nor amphetamine sulfate should be sold over the counter to whoever wishes to employ them, they are powerful chemicals, with the capacity to injure as well as to help. I believe this capacity to injure can be minimized by their combined use, but such administration should be discreetly supervised by a well-qualified physician.

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VENTRICULAR FIBRILLATION AS THE MECHANISM OF SUDDEN DEATH IN PATIENTS WITH CORONARY OCCLUSION*

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ALMOST as characteristic as the attacks of pain in patients with coronary artery disease is the tendency to sudden, unexpected death. Its unpredictable occurrence usually comes as a terrible shock not only to the relatives of the patient but frequently to the physician as well. Particularly disconcerting is the frequency with which autopsy findings fail to explain the sudden death in these cases.

In an attempt to determine the possible clinical factors or structural myocardial lesions sufficient to cause sudden death, 37 cases of coronary occlusion were selected from the files of the Pathological Department of the Rhode Island Hospital in which death had occurred suddenly and unexpectedly. All cases in which associated disease was sufficient to cause death and in which congestive failure was demonstrable clinically or pathologically were excluded.

On analyzing the circumstances attending the fatal seizure, it was found that 31 of the patients were lying in bed either quietly or talking to one of the attendants at the time, 2 were being examined, 1 was on a bedpan, 1 was in the midst of a severe paroxysm of coughing, 1 was being wheeled to the ward and 1 was getting dressed to go home. Of interest was the fact that the cases of ruptured ventricle found at autopsy occurred in the patients who were lying quietly in bed.

Four of the patients were known to have diabetes mellitus. In 2 of these cases a toe had been amputated for gangrene, and in 1 large doses of insulin and intravenous fluids were being administered at the time of death. As a result of clinical and experimental observations it is now recognized that insulin hypoglycemia is dangerous in patients with coronary artery disease, and we are

forced to consider this as a possible contributory factor in this patient's sudden death.

Nine of the patients were receiving digitalis in therapeutic doses during the period immediately preceding their death. The usual objections which have been raised to the use of digitalis in patients with coronary occlusion are that the increase in force of contraction tends to rupture the infarcted heart muscle, and that digitalis predisposes to ventricular tachycardia, increases the work of the heart and constricts the coronary vessels. Gold¹ has pointed out the fallacies in these objections, and it is interesting that although in 3 of the autopsied cases a ruptured heart was found and in 2 cases the electrocardiograms revealed ventricular tachycardia, neither of these occurred in the patients receiving digitalis.

Electrocardiograms had been taken on 20 patients. Single or serial tracings were characteristic of a recent coronary occlusion in 12 cases and the remainder revealed evidence of severe myocardial damage. Transient complete and partial heart block were observed in 1 case, bundle-branch block in 2 and intraventricular conduction defect in 4. Auricular fibrillation and ventricular tachycardia were each noted in 2 cases, and multiple ventricular ectopic beats from several foci were present in 4. Since the experimental production of ventricular fibrillation in animals is frequently preceded by numerous extrasystoles and ventricular tachycardia, the presence of these arrhythmias was considered as having an important bearing on the incidence of sudden death.

Pathologically most of the hearts were enlarged, the range being from 300 to 750 gm., with an average of 475 gm. Intracardiac thrombi were found in the left ventricle in 6 cases, in the right ventricle in 1 and in the right auricle in 3. Thrombotic occlusion occurred in 29 cases and arteriosclerotic narrowing in 8. All the latter revealed evidence of recent or old myocardial infarction.

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Coronary sclerosis was present from moderate to marked degree in all cases. Occlusion in the thrombotic cases involved the anterior descending branch of the left coronary artery, the left circumflex, the right circumflex and the main right in that order. Structurally the myocardium revealed gross or patchy fibrosis in 20 cases, myomalacia cordis in 6, fibrosis and myomalacia in 8 and rupture of the left ventricle in 3.

With the exception of the relatively small num

Drawing inferences from the relative frequency of ventricular fibrillation following experimental ligation of the coronary arteries in animals, numerous investigators have suggested this as the mechanism of sudden death. In human beings, however, the recorded tracings of ventricular fibrillation taken during sudden fatal attacks are for obvious reasons very rare. This particular disorder of rhythm is a finding strictly within the realm of electrocardiography, since there are no

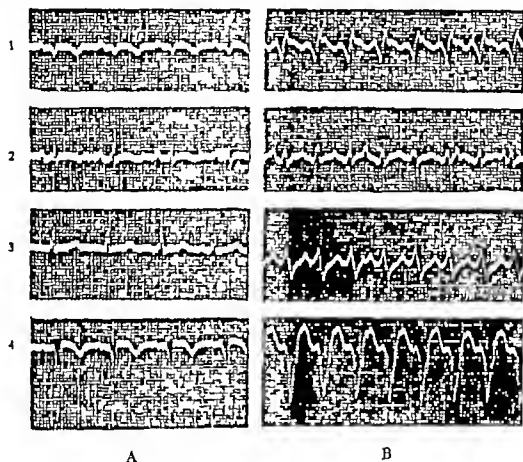


FIGURE 1 Case 1

A Segments of tracings showing inversion of T waves in Leads 1 and 2 with upward convexity of the R-ST portion (coronary T wave of Pardee) and absent R and inversion of T wave in precordial lead

B Electrocardiogram taken during paroxysmal ventricular tachycardia.

ber of cases in which a rupture of the myocardium was found, autopsy observations failed to explain the sudden death, in fact the heart appeared compatible with the continuance of a fairly efficient circulation. This discrepancy between pathologic anatomical and pathologic physiological manifestations has led to several hypothetical explanations of the mechanism of sudden death in patients with coronary artery disease. It has been explained variously by Allbutt² as reflex vagal inhibition" and ventricular standstill by Leary³ as coronary spasm", by Levy and Bruenn⁴ as acute fatal coronary insufficiency", and by Bean⁵ as a "cerebral effect on the vital centers depending on reflexes from a damaged heart. Though interesting these theories have received little support.

diagnostic signs by which it may be detected. Furthermore, the suddenness with which death usually follows the onset of this arrhythmia renders opportunities for graphic recordings very scarce. Hamilton and Robertson,⁶ Levine⁷ and Vela⁸ have reported tracings taken on patients who died suddenly during attacks of angina pectoris, and Meyer⁹ and Calandre and Rodriguez¹⁰ have published records obtained on patients with myocardial failure who died suddenly while electrocardiograms were being taken. In each of these cases, the tracings revealed ventricular fibrillation. Reid¹¹ and Penati¹² have also recorded tracings on patients with cardiac decompensation and auricular fibrillation who developed ventricular tachycardia; the electrocardiograms at death revealed ventricular fibrillation.

It is the purpose of this communication to add to the literature the unusual electrocardiographic findings in 3 patients with coronary occlusion who died suddenly

CASE 1 A R, a 42 year-old man, 2 weeks before admission was taken with a severe "crushing" substernal pain, associated with dyspnea, sweating and weakness and lasting for 24 hours. On examination the first heart sound was barely audible, and the rate was 84. The blood pressure was 100/70. Two days after entry the patient de-

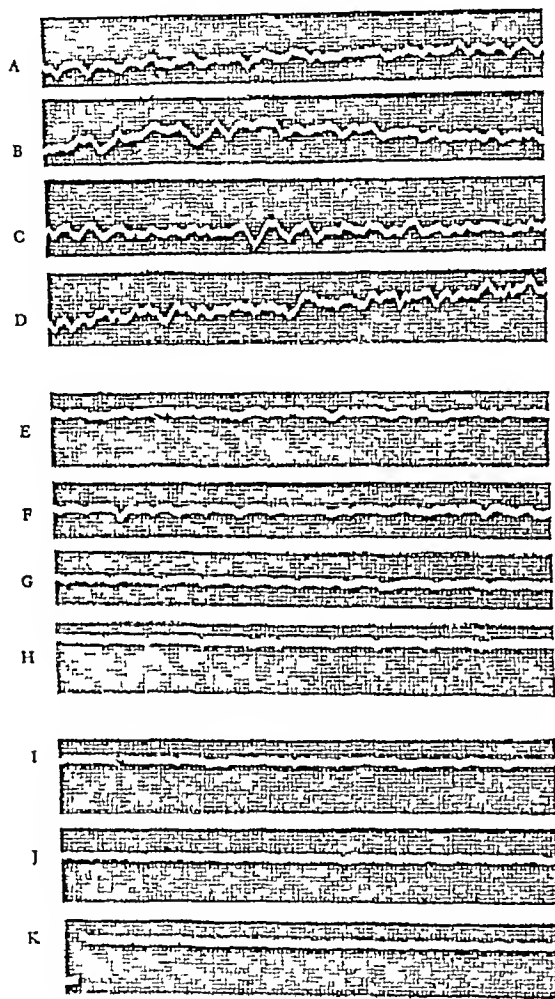


FIGURE 2 Case 1

Segments of electrocardiogram taken at various stages during course of ventricular fibrillation occurring at death

veloped a heart rate of 160, essentially regular but with slight changes in rhythm and variations in intensity of the first heart sound. Approximately 10 minutes after an electrocardiogram was taken the patient suddenly collapsed while talking to a nurse. When seen a few seconds later he was unconscious, markedly cyanotic and gasping spasmodically. The muscles of the left side of his face and left forearm twitched for several minutes. The heart beat could not be detected at any time. The final tracing was taken a few minutes after the patient was pronounced dead.

Autopsy revealed a fibrinous pericarditis and throm-

bosis of the anterior descending branch of the left coronary artery, with infarction of the anterior wall and apex of the left ventricle and part of the interventricular septum. There was a soft mural thrombus at the apex of the left ventricle.

An electrocardiogram (Fig 1A) taken on March 13, 1939, shows a sinus mechanism, a rate of 87, a conduction time of 0.16 sec. and a low Q-R-S voltage. Lead 1 shows an absent R wave, a deep Q wave and an elevation of the S-T junction followed by a sharp inversion of the T deflection. In Lead 2 the S-T segment is rounded, and the T wave slightly depressed. In the precordial lead the R wave is absent, the S-T segment elevated, and the T wave inverted. The record is quite characteristic of an infarction of the anterior wall of the left ventricle. A tracing (Fig 1B) taken at 10:30 a.m. on March 14 reveals ventricular tachycardia, with a ventricular rate of 157 and an auricular rate of 107. In Figure 2, A, B, C and D, are the four leads of the tracing taken at 10:40 a.m., within a few minutes after the patient's sudden collapse; E, F, G and H are strips of records taken at 3-minute intervals, and I, J and K the three standard leads taken at 10:55 a.m. The tracings reveal the diphasic undulations of unequal height, without any of the usual characteristics of the normal electrocardiogram. The ventricular waves gradually decrease in amplitude, but the final strip still shows electrical activity.

CASE 2 A H, a 45 year-old man, had a history of angina pectoris for 2 months previous to admission. On the morning of the day of entry, following strenuous activity, he developed a sudden, very severe "pinching" pain over the precordium, with numbness and weakness of the left arm, he perspired profusely and felt very weak. On examination the heart sounds were of good quality, the rate 60, and the blood pressure 110/70. In the hospital the patient had several attacks of severe precordial pain. On the 34th hospital day, approximately 2 hours after another severe attack of precordial pain, the patient was connected up for an electrocardiogram. He appeared comfortable at the time. Suddenly he gasped and fell back unconscious. The pulse and heart action were imperceptible, but the patient continued to gasp spasmodically for several minutes.

Figure 3 represents electrocardiograms taken at intervals during the patient's hospital stay. In A there is a sinus mechanism, a rate of 59, a conduction time of 0.15 sec., and inversion of T waves in Leads 2 and 3. In B there is a sinus mechanism, a rate of 72, and a conduction time of 0.16 sec., the S-T segment is slightly depressed in Lead 1 and elevated in Leads 2 and 3, and a conspicuous Q wave is present in Lead 2 as well as in Lead 3. The development of the deep Q waves and the T-wave changes are consistent with the diagnosis of coronary occlusion. In C there is a sinus mechanism, and a rate of 68, this tracing is similar to the original record except for the prominent Q wave in Lead 2. Figure 4 represents three records taken during the last attack. The electrocardiogram was started almost immediately after the patient became unconscious. The tracings, continued for 10 minutes after the patient had been pronounced dead, display the unco-ordinated undulations characteristic of ventricular fibrillation. At first quite well marked, these undulations gradually became more irregular and decreased in amplitude until a straight line was recorded.

CASE 3 P S, a 58 year-old man, had a history of exertional dyspnea for over 2 years. Sudden severe vise-like pain over the midsternum associated with weakness of both forearms developed 4 days before entry. Perspiration,

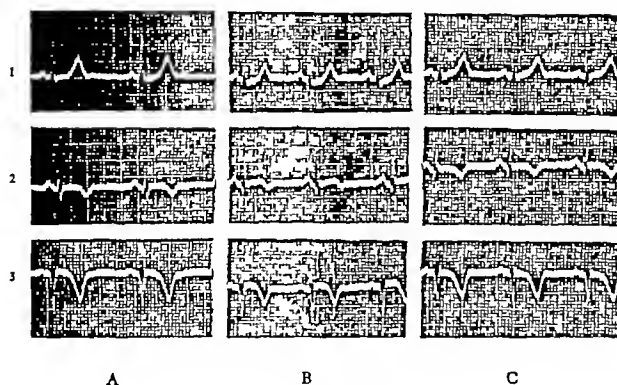


FIGURE 3. Case 2

A B C Sections of the three standard leads of the electrocardiogram taken at intervals during patient's illness showing left-axis deviation depression of S-T segment in Lead 1 and elevation in Lead 3 with inversion of T waves in Leads 2 and 3

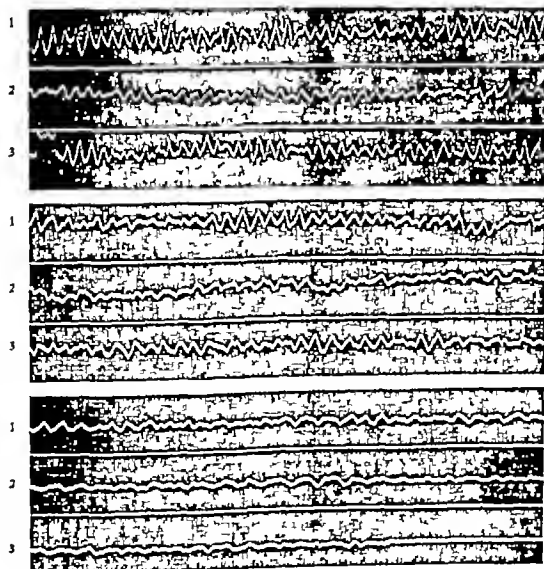


FIGURE 4 Case 2

Segments of electrocardiogram taken during patient's sudden collapse showing ventricular fibrillation

dyspnea and angor animi were present. On examination there were moist rales at both bases. The heart sounds were barely audible. The blood pressure was 110/80. Approximately 2 hours after admission the patient raised

transition from the pre-existing curves to ventricular fibrillation, it is sufficiently significant that the electrocardiographic studies obtained on these pa-

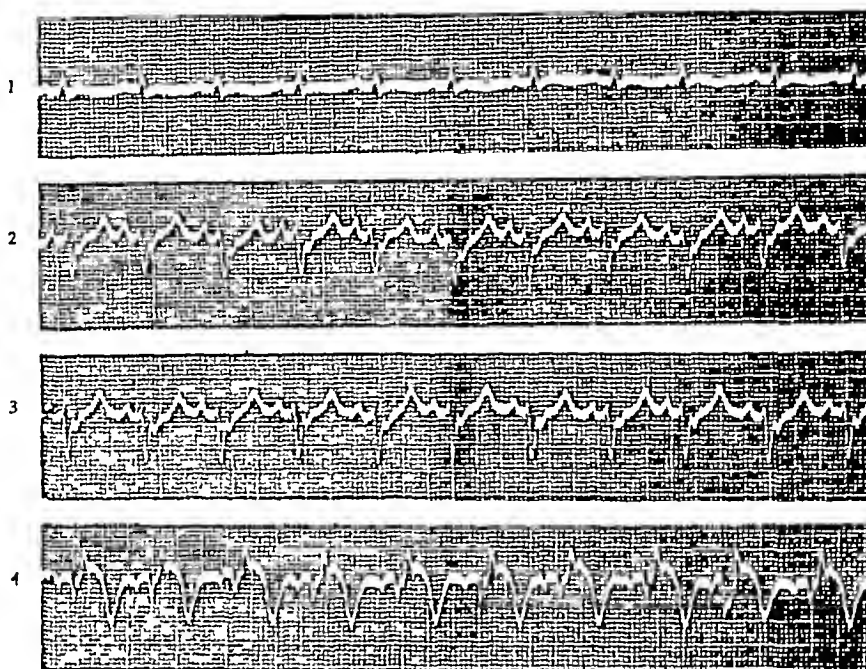


FIGURE 5 Case 3

Tracings show left-axis deviation, intraventricular conduction defect, coronary T wave type of deviations in Leads 1 and 4

himself to speak to the nurse and fell back unconscious. Cyanosis rapidly appeared, gasping respirations persisted for several minutes and froth appeared at the corners of the mouth. There was no evidence of cardiac activity at the apex or wrist when the patient was seen by the ward physician a few minutes later.

Figure 5 shows the electrocardiogram taken on April 10, 1939, shortly after hospital entry. Action is regular except for sinus arrhythmia. The conduction time is 0.16 sec., and the rate 93. The Q-R-S complexes are notched and widened to 0.16 sec., indicating an intraventricular conduction defect. In Lead 1 the S-T segment is rounded and the T wave dipping. In Leads 2 and 3 the T waves are upright. In the precordial lead the R wave is absent, the S-T segment elevated, and the T wave deeply inverted. The record is characteristic of infarction of the anterior wall of the left ventricle. Figure 6 represents electrocardiograms taken on April 10, 1939. The record was started approximately 5 minutes after the patient's unexpected death and shows strips of tracings taken at 1 minute intervals. The electrocardiographic oscillations of varying amplitude, regularity and frequency are quite typical of fibrillation of the ventricles.

DISCUSSION

The chief reason for placing these electrocardiographic curves on record is that they seem to be of utmost significance in elucidating the nature of the mechanism responsible for sudden death in some patients with coronary artery disease. Although none of the records show the direct

tients shortly after sudden death revealed fibrillation of the ventricles.

Clinically, these three cases presented certain features in common. The patients were middle-aged men, aged respectively forty-two, forty-five and fifty-eight. The signs and symptoms at the onset and the electrocardiograms were quite typical of coronary occlusion. In each case death was very sudden, occurring on the sixteenth, thirty-fourth and fourth day after the original attack. With the onset of the lethal attack the patients rapidly became cyanotic and breathing became stertorous and irregular, and in one case inco-ordinate twitchings of the skeletal muscles were noted. In no case was there any evidence of heart action at the apex or at the radial pulse.

The tracings in Figures 2, 4 and 6 are similar to those previously published as examples of ventricular fibrillation. The electrocardiographic oscillations are at first fairly large and in Figure 4 quite regular. The amplitude then gradually decreases, the deflections become irregular and less frequent, until toward the end only small oscillations are recorded. Of interest in Cases 1 and 3 are the modification of the records by smaller waves which are probably due to auricular activity. Wiggers,¹³ in his study of ventricular

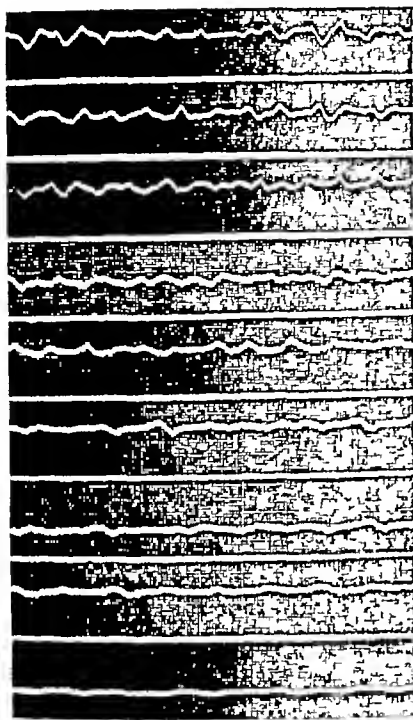


FIGURE 6. Case 3

Segments of tracings taken at various intervals following the patient's sudden collapse

fibrillation in dogs, noted that the auricles could maintain their rhythm for varying intervals, the contractions at times terminating before cessation of ventricular fibrillation and at other times outlasting the fibrillation. In our tracings, auricular activity was still evident long after fibrillation had ceased.

Case 1 is particularly interesting in that it shows the rarely recorded sequence of an ectopic tachycardia arising in the ventricle and superseded by ventricular fibrillation and death.

SUMMARY

Necropsy observations in 37 cases of coronary occlusion failed to explain the sudden death in all but 3 cases.

Three cases are reported in which ventricular fibrillation was found to be the cause of sudden death in patients with recent coronary occlusion.

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REPORT ON MEDICAL PROGRESS

CHEMOTHERAPY AND SEROTHERAPY OF PNEUMONIA

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SYNTHESIS of the azo dyes in the dye industry is responsible for the production of para-aminobenzenesulfonamide, for which the non-proprietary name, "sulfanilamide," was adopted.¹ Encouraging results against pneumococcal infection with sulfanilamide led to the development of the pyridine derivative, 2-(*p*-aminobenzenesulfonamido) pyridine. In May, 1938, Whitby² demonstrated its therapeutic value against experimental hemolytic streptococcal, meningococcal and pneumococcal infections in mice. The designation, "sulfapyridine," has been adopted.³

IN VITRO AND ANIMAL EXPERIMENTS

In vitro experiments indicate that sulfanilamide and sulfapyridine are capable of inhibiting the growth of pneumococci and that this bacteriostatic action is enhanced in the presence of specific antipneumococcus serum.

Sulfanilamide and sulfapyridine are capable of delaying death and, in some cases, of saving the life of animals inoculated with otherwise fatal doses of pneumococci. Sulfapyridine is more effective in this respect than sulfanilamide. In animal experiments the combined use of sulfanilamide and specific antipneumococcus serum has proved more effective against pneumococcal infection than has the administration of either alone.

SULFANILAMIDE IN PNEUMOCOCCAL PNEUMONIA

The controlled series of cases of pneumococcal pneumonia treated with sulfanilamide by Price and Myers⁴ is of special significance. An attempt was made to maintain the blood concentration between 7 and 15 mg per 100 cc. and preferably above 10 mg. Of 115 treated cases, 18, or 16 per cent, died, and of 94 controls, 29, or 31 per cent, died. Comparison of the treated cases with the controls suggests that the favorable results are to be ascribed to the use of sulfanilamide.

A severe hemolytic anemia developed in 6, or 5 per cent, and a moderate secondary anemia in an additional 21, or 18 per cent, of the patients treated with sulfanilamide. Toxic hepatitis developed in 1 patient.

Of 81 collected cases of Type 3 pneumococcal pneumonia treated with sulfanilamide,⁴⁻¹² 24, or 30 per cent, died. Though this fatality rate is

considerably lower than the expected rate of about 50 per cent in this type of infection, a larger series will be necessary before the merit of the drug in the treatment of cases with Type 3 pneumococcal pneumonia can be regarded as established.

Though there is merit in the use of sulfanilamide in the treatment of pneumococcal pneumonia, it is less effective and more likely to produce toxic effects than is sulfapyridine.

SULFAPYRIDINE IN PNEUMONIA

Reports¹³ on the use of sulfapyridine in a large number of cases of pneumonia have been published. In the reports by Telling and Oliver,¹³ Evans and Gaisford,¹⁴ Christie,¹⁵ Dyke and Reid,¹⁶ Lawrence,¹⁷ Anderson and Dowdeswell,¹⁸ Agranat, Dreosti and Ordman,¹⁹ Flippin, Lockwood, Pepper and Schwartz,²⁰ Whittemore, Royster and Riedel,²¹ Meakins and Hanson,²² Plummer and Ensworth,²³ Graham, Warner, Dauphinee and Dickson,²⁴ Alsted,²⁵ Gaisford,²⁶ Finland, Spring, Lowell and Brown,²⁷ Pepper, Flippin, Schwartz and Lockwood,²⁸ Cutts, Gormly and Burgess,²⁹ and Long and Wood,³⁰ there is a total of 1612 cases, with 102 deaths or a mortality rate of 6.3 per cent. The series as a whole includes cases in adults classed as lobar pneumonia and of pneumonia without specification as to the form of the disease. Various types of pneumococci were demonstrated as the inciting agents in a considerable proportion. In certain cases, pneumococci were found but were not typed or were non-typable. In some, no pneumococci were found. In a small proportion, other organisms may have been the cause of the process.

The expected death rate in drug-treated cases must be estimated at a somewhat higher figure than 6.3 per cent, probably about 7 per cent, owing, as noted later, to unusual conditions in the African cases reported by Anderson and Dowdeswell¹⁸ and by Agranat, Dreosti and Ordman.¹⁹

Although the 1612 cases cover only about one year's experience, the large size of the series and the widely separated sources suggest that it may, with the exception of the African cases, be regarded as representative. Excluding these from consideration, the expected death rate in similar cases without drug treatment may be estimated at about 25 per cent. Comparison of the

results in drug-treated cases with those in simultaneous controls without the drug, but otherwise similar, confirms the merit of the method.

Favorable results in controlled cases of pneumonia treated with sulfapyridine have been reported from England, Africa and Canada. Pneumococci were not demonstrated as the cause in all cases. In the combined series of Evans and Gaisford (Birmingham),¹⁴ Anderson and Dowdeswell (Nairobi),¹⁵ Agranat, Dreoski and Ordman (Johannesburg)¹⁶ and Graham Warner, Dauphinee and Dickson (Toronto)¹ there are 460 cases treated with sulfapyridine, with 20 deaths or a mortality rate of 4.3 per cent, against 450 not so treated, with 69 deaths or a rate of 15.3 per cent. Comparison of the treated and control groups suggests that the age distribution and the type of pneumococcal infection are not the explanation of the more favorable result in the treated cases. The treated and control groups, as a whole, do not, however, represent random samples of the population, and equally favorable results are not ordinarily to be expected. The unusually low death rate in both groups is due to the inclusion in the series of a large number of African patients, namely 330 in the treated and 320 in the control groups, a very large proportion of whom were selected males twenty to forty years of age and some of whom had been previously vaccinated against pneumococci. In consequence, these African cases are omitted from all of the following series of cases.

SULFAPYRIDINE IN PNEUMOCOCCAL PNEUMONIA

In the series of 1612 cases, there are 974 of pneumococcal pneumonia,* with 65 deaths or a mortality rate of 6.7 per cent. In general, it may be estimated that the expected death rate in pneumococcal pneumonia without drug or antiserum therapy ranges from 25 to 30 per cent. In Bullowa and Wilcox's¹⁰ series of 1515 cases of pneumococcal pneumonia (including lobar pneumonia and bronchopneumonia) there were 379 deaths, a rate of 25 per cent.

SULFAPYRIDINE IN PNEUMONIA DUE TO SPECIFIC TYPES OF PNEUMOCOCCI

Variation in the efficiency of chemotherapy against experimental pneumococcal infection in animals has been attributed to the individual strain,^{21, 22} rather than to the type differences of the organism. The results with sulfapyridine in the treatment of pneumococcal pneumonia appear to be favorable with all types of infection. The number of treated cases due to individual types is, however, sufficiently large for separate con-

sideration in only two. Of 288 treated Type 1 cases, there were only 15 deaths, this gives a mortality rate of 5.2 per cent, against an expected rate of about 30 per cent. Of 210 Type 3 cases there were only 18 deaths, a rate of 8.6 per cent, against an expected rate of about 50 per cent. The results with Type 3 are especially significant, owing to the ineffectiveness of specific antiserum in the treatment of pneumonia due to this type. Further evidence is desirable regarding the merit of the drug in statistically significant numbers of cases of pneumonia due to other specific types of pneumococci. Of 74 Type 2 cases, there were 3 deaths, a rate of 4.1 per cent against an expected rate of about 43 per cent. More information should also be obtained regarding variations in the resistance of different strains of pneumococci to sulfapyridine.

CAUSES OF FAILURE IN CHEMOTHERAPY

In reviewing the reports of the findings in fatal cases, it is obvious that many were inevitable failures. In some, cardiac or renal complications played an important part in the death of the patient. In others, chemotherapy was inaugurated late in the course of the disease and the infection had already involved the pleura or meninges or progressed to such a stage that the patient was moribund on admission.

The age of the patients influenced the results to an important degree. Of 880 collected drug treated cases, 649 were forty-nine years of age or under with 14 deaths (2.2 per cent) and 231 were fifty years of age and over, with 44 deaths (19.0 per cent). The greater seriousness of the disease as age advances may be ascribed to diminished resistance against the pneumococcus and hence a greater tendency toward generalization of the infection.

Blood cultures were taken in only a small proportion of the reported cases, and on the whole the percentage with bacteremia was low. Of 93 cases with positive blood cultures, 22 or 24 per cent died.

It may be assumed that the results with sulfapyridine in the treatment of pneumococcal pneumonia fall short of an attainable goal. Earlier drug therapy would probably have saved a still larger proportion. The higher fatality rate in patients in the older age group and especially in bacteremic cases suggests that reliance on sulfapyridine alone is undesirable when the outlook is known to be relatively poor and that, in severe cases due to specific types of pneumococci for which antiserum is available and contraindications are absent, treatment with antiserum should be combined with chemotherapy.

* This group are included 11 cases in which pneumococci were found. In certain instances other organisms which may have been of significance were also found.

INFLUENCE OF SULFAPYRIDINE ON THE CLINICAL COURSE OF PNEUMONIA

One of the most impressive effects of treatment of pneumococcal pneumonia with sulfapyridine is the fall in the temperature to normal within twenty-four to thirty-six hours in a large proportion of cases. Not infrequently it again rises to a low grade of fever. The fall in the temperature is accompanied by an improvement in the patient's general condition, but this improvement is more gradual than it is after a normal crisis. Failure of the temperature to fall suggests the presence of a complication or some inciting agent other than the pneumococcus.

No immediate change in the physical signs is to be expected, and the area of consolidation runs its usual course. Some extension of the pulmonary process occurs in a small proportion of cases. The length of stay in the hospital is less in drug-treated than in control cases.

The influence of sulfapyridine on the occurrence of serofibrinous effusion and empyema as a complication is uncertain. On the whole, the evidence suggests some reduction under chemotherapy in the proportion of cases with empyema.

TOXIC EFFECTS OF SULFAPYRIDINE

The commonest toxic effects of sulfapyridine are nausea and vomiting, which in adults are likely to be present in almost all cases. Vomiting occurs in about two thirds of the cases and is sufficiently troublesome to interfere with the treatment in about 10 per cent. Mental and physical depression and delirium occur in some cases. Cyanosis is much less often observed with sulfapyridine than it is with sulfanilamide. Dermatitis has occurred in rare instances.

Severe blood changes in the course of treatment of pneumonia with sulfapyridine are much less frequent than they are with sulfanilamide. Agranulocytosis is reported in 1 of 50 cases reported by Graham, Warner, Dauphinee and Dickson.²⁴ The patient had been treated for nineteen days with a total of 79 gm of sulfapyridine. Interruption of the drug was followed by improvement, and at the time of the report the patient was making a satisfactory recovery. Agranulocytosis is reported in 1 of 27 Europeans in the Johannesburg series by Agranat, Dreosti and Ordman.¹⁰ Marked leukopenia developed in 2 of Pepper, Flippin, Schwartz and Lockwood's²⁸ 400 cases, but no instance of agranulocytosis was observed. Two patients developed agranulocytosis in the third week of drug therapy in Long and Wood's⁴⁶ series of 100 cases. One recovered and the other died. A third developed a severe leukopenia with return of the white cells to normal after

the drug was stopped. One fatal case of agranulocytosis, in a nineteen-year-old boy, is reported by Finland, Spring, Lowell and Brown,²⁷ but the case is not included in their series as no pneumococci were found in the sputum. Following drug therapy there was a total absence of granulocytes in the blood within thirty-six hours and death within forty-eight hours.

A moderate fall in the hemoglobin and red count may be expected in severe cases of pneumonia in consequence of the infection. In several cases Pepper, Flippin, Schwartz and Lockwood²⁸ observed a drop in the red-cell count of over 2,000,000, with a reduction in the hemoglobin of as much as 40 per cent. In their series of 400 typed cases treated with sulfapyridine there was 1 patient with acute hemolytic anemia, with apparent recovery. Two instances of acute hemolytic anemia in Negroes occurred in Long and Wood's⁴⁶ series.

Nephritis has not been observed as a result of treatment with sulfapyridine, and the drug has been given without harmful results in the presence of nephritis. Pepper, Flippin, Schwartz and Lockwood²⁸ treated one patient with pneumococcal pneumonia and acute nephritis. After recovery from the pneumonia, there was rapid improvement in the nephritis and after five days of drug therapy, the urine showed no red blood cells, only a faint trace of albumin, and the level of blood urea-nitrogen steadily improved. In 12 fatal cases in their series, sections of the kidneys failed to show any changes from the normal other than those to be expected in an acute febrile illness.

Hematuria is to be expected in a small proportion of cases of pneumonia without drug treatment. In Pepper, Flippin, Schwartz and Lockwood's²⁸ 277 cases with urinalysis during treatment, hematuria was discovered after initiation of sulfapyridine therapy in 14, or 5.4 per cent, against an expected rate of perhaps 4 per cent. The hematuria in most cases was observed in only one or two specimens and often disappeared during continuance of the drug.

Gross hematuria, of more serious import, may be due to irritation by crystals of acetylsulfapyridine. The formation of uroliths in the urinary tract of animals fed with sulfapyridine was observed by Antopol and Robinson³³ and by Gross, Coover and Lewis.³⁴ Gross hematuria, usually with ureteral pain, was noted in 4 of the 50 cases reported by Graham, Warner, Dauphinee and Dickson.²⁴ The blood disappeared in a few days without residual damage to the kidney. Gross hematuria was noted in 3 of the 381 cases reported by Pepper, Flippin, Schwartz and Lockwood.²⁸ Southworth and Cooke³⁵ cite 3 cases of hematuria, 1 with visible blood, under treatment with sulfapyridine,

in 2 of the 3 there was severe abdominal pain, and in 2, nitrogen retention due to renal insufficiency. In Long and Wood's⁴⁴ 100 cases, there was 1 with gross hematuria. This was first observed on the sixth day of treatment and the drug was immediately discontinued. The urine decreased in amount. Numerous boat shaped and spearhead brownish crystals were noted, and the blood non protein nitrogen was elevated. At autopsy hundreds of small calculi made up largely of acetyl sulfapyridine were found in both kidney pelvises and ureters. Histological sections of the kidneys and ureters did not show abnormalities which could be attributed to stone formation. The suspicion may, however, be entertained that there was urinary obstruction. They found that practically all patients on the drug have acetylsulfapyridine crystals in the urine but were unable to correlate the number of crystals in the urine with the appearance of hematuria. In the case reported by Tsao, McCracken, Chen, Kuo and Dale⁴⁵ the death of a boy of eight is attributed to uremia in consequence of bilateral complete urinary obstruction by uroliths following treatment with sulfapyridine.

ADMINISTRATION OF SULFAPYRIDINE

In cases of pneumonia in which chemotherapy is under consideration it is desirable to obtain material with which to determine the inciting agent before the administration of the drug. A gram stained smear of the sputum should be examined to determine the presence and number of organisms. Pneumococci should be typed by the usual procedures. Owing to the occasional difficulty of making a distinction between pneumococci and streptococci by morphology and staining reaction, cultures should be made on blood agar plates, and if necessary, the organism tested for bile solubility. If no sputum is available, the inciting agent may be determined by the examination of material obtained with a pharyngeal or laryngeal swab.

Owing to the bacteriostatic effect of chemotherapy, the growth of organisms in the blood may be prevented and it is therefore desirable to take a blood culture as a routine before sulfapyridine is administered. In cases in which the response to drug treatment is not favorable, subsequent blood cultures should be taken.

In view of the possibility of toxic reactions after chemotherapy, the blood should be examined before the treatment is begun and at frequent intervals thereafter. The examination should include determinations of the hemoglobin and of the red cell white-cell and differential counts. Sulfapyridine should not be given in the presence of hemolytic anemia or agranulocytosis. It is desir-

able to obtain further information concerning the dangers, if any, of giving the drug in the presence of jaundice or impaired liver or kidney function. If dermatitis occurs, it is desirable to stop the drug.

The urine should be examined before and during the treatment. Determination of the amount of nonprotein nitrogen in the blood is also desirable. As previously mentioned, the chief danger of the drug with respect to the urinary tract appears to be obstruction from the formation of crystals of acetylated sulfapyridine. Although blood in the urine may occur in consequence of the infection its presence in any considerable amount may be regarded as a danger signal. Gross hematuria, ureteral pain and evidence of urinary obstruction are indications for discontinuance of the drug.

There is a group of cases with atypical pneumonia running a mild course with low white counts, without significant numbers of pneumococci in the sputum and possibly of virus origin in which the use of the drug is not indicated.

For adults, the initial dosage of sulfapyridine is 2 gm., followed by 1 gm. every four hours. It is desirable to continue this dosage until the temperature has been normal for thirty six or forty eight hours. Since cessation of treatment at this time may be followed by a lighting up of the infection it is desirable to continue with 1.0 gm. every six hours until resolution is well under way and then to give 0.5 gm. four times daily until the lungs are clear. The total amount necessary is likely to vary in different patients within rather wide limits, but in general from 16 to 25 gm. may be expected to be sufficient. With a spreading lesion or with bacteremia, from 25 to 50 gm. may be necessary.

Sulfapyridine appears to be better tolerated if the tablets are crushed and taken with water, milk or fruit juice and with 0.6 gm. (10 gr.) of sodium bicarbonate. With troublesome nausea and vomiting phenobarbital or barbitol may be helpful, and to prevent dehydration and maintain a balance of electrolytes intravenous physiologic salt solution and glucose are desirable. The drug should, if possible, be continued in spite of vomiting. If a dose is vomited it should be repeated. Though there is no evidence that cyanosis is due to the formation of sulfhemoglobin it is suggested that sulfur-containing drugs be avoided during the administration of sulfapyridine. Owing to the development of dermatitis following exposure to ultra violet irradiation in a case under treatment by Hallam,⁴⁶ further evidence should be obtained regarding the influence, if any of exposure to sun light or any form of artificial sunlight during administration of the drug.

Other than oral administration of sulfapyridine

is not practical, because of the very slight solubility of the drug. A soluble sodium salt of sulfapyridine, described by Marshall, Bratton and Litchfield³⁷ and investigated in experiments in dogs and patients with pneumonia by Marshall and Long,³⁸ may be given intravenously. Long and Wood⁴⁰ calculate the dosage on the basis of 0.06 gm per kilogram of body weight, and the drug is made up in a 5 per cent solution with sterile distilled water. They state that sodium sulfapyridine is unstable to heat and cannot therefore be sterilized, but that the 5 per cent solution with a pH of 10.7 to 10.8 is itself somewhat bactericidal. Preparation of the solution from the drug dispensed by the manufacturer in sterile ampules would seem preferable. If the solution gets outside the vein a bad slough may result. The injection should be made slowly, at the rate of 5 cc per minute. Intravenous therapy may be used to supplement administration of sulfapyridine by mouth if absorption from the gastrointestinal tract is poor or the patient severely ill. It may also be used in the treatment of patients who cannot retain sulfapyridine because of vomiting. Nausea and vomiting follow intravenous as well as oral therapy, but effective blood concentrations may thus be obtained. The intravenous dose may be repeated at intervals of six or eight hours.

Gaisford, Evans and Whitelaw³⁹ find from an experience with over two hundred injections that the sodium salt of sulfapyridine can be given intramuscularly in a 33 per cent solution (1 gm in 3 cc) with only slight risk of ulceration at the site of injection. The solution should be injected deeply into the gluteal muscles, with as little escape along the needle tract as possible. In their experience, intramuscular is preferable to intravenous injection, being easier for general use, less likely to cause vomiting, and equally satisfactory with respect to the blood concentration of the drug.

BLOOD CONCENTRATION

Greey, MacLaren and Lucas⁴⁰ find that in the treatment with sulfapyridine of pneumococcal infections in mice a high percentage of survivors was obtained only when the blood concentration was kept above 10 mg per 100 cc for several days. In man, lower concentration may be expected to be effective in consequence of greater natural resistance to pneumococcal infection.

The blood concentration of the drug is found to vary widely among pneumonia patients on the same schedule of dosage. Individual variations in the rate of absorption, in the rate of formation of the inactive conjugated *p*-acetylaminobenzenesulfamidopyridine and in

the rate of excretion may be responsible for this lack of uniformity. There appears to be no definite correlation between the blood concentration and the results thus far obtained, and further evidence concerning this matter is desirable.

RELATIVE MERITS OF SULFAPYRIDINE AND ANTISERUM

Considering only pneumococcal pneumonia, the death rate under treatment with sulfapyridine alone is lower than that with specific antiserum alone. Of the various types of pneumococcal pneumonia treated with the drug, Type-1 cases only comprise a sufficient number to warrant comparison. As already noted, 288 such cases have been treated with sulfapyridine, with a death rate of 5.2 per cent. By contrast, in Cole's⁴¹ 462 Type-1 cases treated with antiserum the death rate was 10.5 per cent, the lowest attained in any large series. The data given are insufficient to compare the two series with respect to age grouping, bacteremia, duration before treatment, alcoholism and extent of lung involvement, but it is unlikely that there are significant differences in these respects in the two series, hence the results are more favorable with the drug than with antiserum. Comparison of the results in Type-1 cases with drug treatment and those in the Massachusetts series⁴² with antiserum is even more favorable to the drug, as the fatality rate in 1451 cases treated with antiserum within the first four days of the illness was 13.3 per cent.

Sulfapyridine has the additional advantage that it is applicable to all types of pneumococcal infection and can be administered by mouth. Precautions in its use involve the application of relatively simple procedures, serious toxic effects are rarely observed.

SULFAPYRIDINE AND ANTISERUM IN PNEUMOCOCCAL PNEUMONIA

There is, thus far, little information with respect to the results in the combined use of sulfapyridine and antiserum. Plummer and Ensworth²³ treated 48 cases with 2 deaths, Pepper, Flippen, Schwartz and Lockwood²⁸ 12 with 2 deaths, and Cutts, Gormly and Burgess²⁹ 13 with 3 deaths—making a total of 73 cases with 7 deaths, a mortality rate of 9.6 per cent. Details regarding the cases are lacking, and the possibility cannot be excluded from the data given that in certain instances a combination of the two types of therapy was used in the more severe cases. Of the 80 cases selected for treatment with the drug and antiserum in Finland, Spring, Lowell and Brown's²⁷ series, 81 per cent were over the age of forty and 34 per cent over sixty. Bacteremia was present in 40 cases, or 50 per cent. The pneumonia was due to the Type-1 pneumococcus in 33

cases, Type 2 in 17, Type 3 in 16, Type 5 in 4, Type 7 in 3, Type 8 in 3 and other specific types in 4. Of the 80 cases, 21 patients died, or 26 per cent. These results with combined sulfapyridine and specific antiserum are not comparable with their results in cases treated with sulfapyridine alone in which, of 95 cases, 14 died, a mortality of 15 per cent. Only the milder cases were first chosen for treatment with the drug alone. The expected death rate in similar cases with out specific serum or drug is estimated at 75 to 90 per cent, and with specific serum alone at 50 to 60 per cent. In the combined use of antiserum and sulfapyridine they find that the drug can be dispensed with in periods varying from twelve to thirty-six hours and that with probability much smaller doses of serum are needed than in cases treated without the drug.

In view of the established merit of sulfapyridine in pneumococcal pneumonia and of specific antiserum in certain types of pneumococcal infection it may be assumed that the combination of the two methods of treatment will prove more effective in certain cases than the use of the drug alone.

MECHANISM OF RECOVERY IN TREATED CASES

Though no satisfactory explanation of the therapeutic effectiveness of sulfapyridine in the treatment of pneumococcal pneumonia can be offered, an interplay of two factors may be assumed in the mastery of the invading organism, namely the effect of the drug and the defenses of the host against the pneumococcus.

Regarding the effect of the drug on the pneumococcus, *in vitro* experiments suggest that, in the absence of leukocytes, there is an inhibition of growth or bacteriostasis and no bactericidal action. With sulfanilamide and sulfapyridine *in vitro* there is a short latent period during which no effect is produced, and it seems probable that in the infected host there is first an action on the pneumococcus. This action as suggested by McIntosh and Whitby,⁴² may be due to interference with the metabolic or enzymatic activities of actively growing organisms.

The defenses of the host play a necessary part in recovery. The most significant factors are specific antibodies and free and mobile phagocytic cells. Specific antibodies in the patient's blood have an important bearing on the outcome. With them a large proportion of patients recover and without them a large proportion die. The manner in which they act is imperfectly understood, but they may be assumed to alter the protective covering or capsule and thus prepare the organism for destruction by phagocytic cells.

Until the advent of chemotherapy, the outcome of pneumococcal pneumonia was largely dependent

on the natural resistance of the patient, his power during the course of the disease to elaborate and utilize specific antibodies reinforced by the use of specific antiserum, and his capacity to withstand the ill effects of pneumococcus toxemia. The favorable results with sulfapyridine alone are to be ascribed to the combined effect of the drug and the defenses of the host. Animal experiments indicate, however, that chemotherapy is enhanced in the presence of specific antibody, and the experience in man suggests that better results are to be expected in certain cases with the combined use of sulfapyridine and specific antibody.

SUMMARY AND RECOMMENDATIONS

Advances of great importance have been made in the development of sulfonamide derivatives for the treatment of bacterial infections and especially in the discovery of the merit of sulfanilamide and sulfapyridine in pneumonia therapy. Of these substances, sulfapyridine is more effective and less likely to give rise to toxic effects than is sulfanilamide.

There are reports on the use of sulfapyridine in the treatment of a large number of cases in adults of pneumonia including those classed as lobar pneumonia and pneumonia without specification as to the form of the disease, and a reduction in the fatality rate from about 25 per cent to about 7 per cent may be expected. Age influences the result to an important degree. The fatality rate is only about 2 per cent in patients under fifty years of age and 19 per cent in patients fifty years of age or over.

In pneumococcal pneumonia treated with sulfapyridine, the fatality rate has been reduced from 25 or 30 per cent to 6 or 7 per cent. The drug appears to be effective irrespective of the type of pneumococcal infection. The fatality rates in drug-treated Type 1 pneumococcus pneumonia cases is 5 or 6 per cent as against an expected rate of about 30 per cent, and in Type 3 cases 8 or 9 per cent as against an expected rate of about 50 per cent.

The results in the treatment of pneumococcal pneumonia with sulfapyridine alone are more favorable than they are with specific antiserum alone. Drug therapy earlier in the course of the disease would probably save a larger proportion of the fatal cases.

The combined use of sulfapyridine and antiserum in certain cases will doubtless prove more effective than either alone. The favorable results with sulfapyridine in man are to be ascribed to the combined effect of the drug and the defenses of the host, and it may be assumed that in certain drug-treated cases the production of specific antibody by the patient is not sufficient to overcome

the infection and that under such circumstances the administration of specific antiserum is necessary

In cases in which sulfapyridine is under consideration, it is desirable to obtain material with which to determine the inciting agent before the administration of the drug. If no sputum is available, examination may be made of material obtained on a pharyngeal or laryngeal swab. It is desirable to take a blood culture as a routine before the drug is administered and at suitable intervals thereafter.

In view of the established merit of sulfapyridine in pneumococcal pneumonia, it is desirable to begin treatment with the drug as soon as the diagnosis is established, provided there are no contraindications to its use. In view of the possibility of toxic reactions, the blood should be examined before the treatment is begun and at frequent intervals thereafter. This examination should include determinations of the hemoglobin and of the red-cell, white-cell and differential counts. It is undesirable to administer sulfapyridine in the presence of hemolytic anemia or agranulocytosis. Discontinuance of the drug is desirable in patients who develop a rash. In some cases, vomiting is sufficiently severe to require discontinuance of the drug.

The urine should be examined before and during treatment and determination of the amount of nonprotein nitrogen in the blood is desirable. Gross hematuria, ureteral pain and evidence of urinary obstruction are indications for discontinuance of the drug.

With pneumonia due to specific types of pneumococci in which sulfapyridine cannot be used, specific antipneumococcus serum, with due precautions in the use of an alien serum, is desirable.

Specific antiserum may well be held in reserve and given, with due precautions, in cases in which chemotherapy is begun early in the disease and in which the pulse, respirations and temperature fail to fall essentially to normal within twenty-four or thirty-six hours. The more immediate resort to combined drug therapy and specific antiserum is desirable under such relatively unfavorable circumstances as in patients with pneumococcal pneumonia over fifty years of age, in the known presence of bacteremia, with multilobar involvement or a spreading lesion or during pregnancy or the first week of the puerperium.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25411

PRESENTATION OF CASE

A forty-eight year-old married American male clerk entered the hospital complaining of shortness of breath.

Five years before entry while cranking an automobile, the patient was suddenly seized with a severe attack of agonizing pain across the upper part of his chest on both sides which radiated down the inner side of both arms and which caused him to stop immediately, get into the car and gasp for breath. The attack lasted about fifteen minutes and then lessened in severity, but a discomfort and shortness of breath remained for the rest of the day. Subsequent to this attack the patient had noted similar but milder episodes which were precipitated by exertion. They were always immediately relieved by rest. With restricted activity the attacks gradually became less in frequency. Two and a half years before entry he began to note dyspnea on climbing stairs. This progressed gradually until one year before admission when he was unable to climb one flight without being short of breath. There was little pain noted during this time. Three months before entry he became dyspneic on merely hurrying as he walked. One week before admission, while asleep, the patient was suddenly awakened gasping for breath so that he was forced to arise and walk for a few minutes before going back to bed. For three or four nights before entry he was afraid to go to bed on account of this distress. Two months before entry swelling of the feet and ankles appeared, and a local physician prescribed pills, decreasing the dosage steadily until the patient was taking one pill a day. In spite of this the edema persisted and even grew worse. One month before entry the patient noted palpitation and increasing orthopnea. He had lost about 17 pounds in the three months before entry and gave his present weight as 125 pounds.

The patient stated that he had had severe growing pains at the age of seven which were accompanied by fever, the pain rendered him unable to move for two weeks. At the age of twenty seven he had had "rheumatic pains" in his legs, some time after a urethral discharge. The latter lasted six months and was cured by a physician. He denied

ever having had syphilis. He stated that his joints had never been swollen, red or hot. He regularly had a bad cold every winter, the last one causing temporary increase of shortness of breath.

The family and marital histories were noncontributory.

Physical examination revealed a well-developed and nourished chronically ill, middle aged man, who was dyspneic, orthopneic and edematous. He was somewhat drowsy and perspiring freely. The fundi were described as being arteriosclerotic. The teeth were carious. The throat was injected, but the tonsils were not remarkable. The heart showed an irregular rhythm with occasional extrasystoles. There was a precordial bulge. A diffuse, forceful wavy apex impulse in the sixth interspace, 13 cm. to the left of the midsternal line, was noted. A systolic thrill was palpable at the base, and the pulses were described as being plateau like. The blood pressure in the right arm was 100 systolic, 50 diastolic, and in the left arm 90 systolic, 50 diastolic. There was a harsh, sharp high-pitched systolic blow at the apex, which was transmitted to the axilla and was followed by a loud, long localized rumbling diastolic murmur at the apex. There was an absence of the aortic second sound at the base with an accentuated pulmonary second sound. A harsh loud, low-pitched, coarse murmur replacing the aortic first sound was heard at the base and was transmitted to the neck. No basal diastolic murmur was heard. Examination of the lungs revealed the presence of many moist rales at both bases. The liver was enlarged 10 cm. below the costal margin in the right midclavicular line and was tender the edge was not sharp. There was massive pitting edema of the sacrum and of the feet, ankles, and shins to the level of the knees. The prostate was tender but not enlarged or otherwise remarkable.

On admission the temperature was 98°F., the pulse 98, and the respirations 20.

Examination of the urine was negative and that of the blood showed a red-cell count of 4,200,000 with 80 per cent hemoglobin, and a white-cell count of 8900 with 77 per cent polymorphonuclears. The stool examination was guaiac negative.

The patient rapidly failed and died twenty-four hours after admission. While in the hospital the temperature rose to 101°F., the pulse fell to 94, and the respirations rose to 24.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND. My first impression is that this is a fairly clear-cut case. The clinical course and the physical signs are adequately described. The first indication of serious impairment of this man's heart occurred five years be-

fore his death and consisted of an attack of severe pain following unusual exertion, with radiation fairly characteristic of a coronary origin. It lasted only fifteen minutes. He was a little upset for the rest of the day, but must have made a fairly good recovery. I should first like to determine the nature of this initial episode. I believe that acute coronary insufficiency offers the best explanation in view of the radiation of pain to both arms and the relatively transient nature of the attack. Did he have a myocardial infarct at this time? Probably not, but rather a transient coronary insufficiency.

What else should we keep in mind? This episode occurred out of a clear sky, apparently during what probably constituted unusual exertion for him. Did this cause a small tear in the aortic intima and a dissecting aneurysm in the media? I think there are several points against that interpretation. First, the duration of the pain seems hardly adequate for a tear or dissection. The radiation of the pain to the arms is reasonably good evidence against such an occurrence, as is also the absence of hypertension. I think then that we can safely discard dissecting aneurysm of the aorta.

Other things may happen to the heart in the stress of unusual strain—a valve may rupture. So far as I know that is usually not a very painful event. It is manifested more by an acute disturbance of the circulation or by an abrupt change of the physical signs in the heart. This patient's subsequent course does not suggest such an occurrence. I think, then, that he did not rupture a valve and probably not a chorda tendineae.

For the next two and a half years he was troubled by substernal oppression clearly related to exertion. So far as one can tell from the description this clearly represents angina pectoris. It is interesting, however, that for the final two and a half years of his life this manifestation of coronary insufficiency was replaced by the signs and symptoms of serious myocardial weakness and failure. Prior to the appearance of general venous congestion, this progressive myocardial failure was manifested by signs of predominantly left ventricular weakness. So much for the clinical course extending over a period of five years.

The past history is of some importance, I believe. He apparently had had rheumatic fever. Ordinary growing pains in children are not associated with fever, nor do such patients find it necessary to remain in bed because of discomfort. It would have been of some academic interest if we had known what his physical signs were some ten years before the onset of his last illness. It seems unlikely that syphilis played any part. Although he had had a urethral discharge in the

past, the physical signs described in the heart do not suggest syphilis to me, nor does the clinical course of his heart failure.

Then we come to the physical examination on admission. He obviously had serious heart failure, and died twenty-four hours after admission to the hospital before he could be completely studied. His heart was definitely enlarged. The forceful apical impulse suggests chronic valvular disease (in the absence of hypertension). One will have to speculate a little as to whether he had auricular fibrillation. This is of some importance in appraising the extent of structural disease present. "The heart showed an irregular rhythm with extrasystoles." I do not know whether that can be interpreted as auricular fibrillation with a well-controlled ventricular rate. He almost certainly had had digitalis from the description of the medicine he had been given in the past. Insofar as the auscultatory and other physical signs relating to his heart are concerned he had all that one would expect with well-marked aortic stenosis. He had a large heart with an obvious systolic thrill at the base, best heard over the aortic area. He had the characteristic type of murmur—a harsh basal systolic murmur transmitted upward. He had an absent aortic second sound in the face of a loud pulmonary second sound, and furthermore, the blood-pressure level and pulse pressure were suggestive, although we have to accept these latter findings with some caution because he had serious heart failure at the time they were determined.

In addition to the signs of aortic stenosis, certain additional physical signs are described at the apex which suggest involvement of the mitral valve. At first glance and on the basis of the apical murmurs alone one might suspect serious involvement of the mitral valve. He had a loud systolic murmur and a rumbling diastolic murmur in this area. We have learned in recent years to be a little cautious in the interpretation of murmurs at the cardiac apex in the presence of a big heart, previously I had often been mistaken. We now know there are certain conditions which may simulate mitral stenosis. Dilation of the heart in children with severe myocardial damage following rheumatic fever has been particularly difficult to evaluate. We know that free aortic regurgitation may occasionally produce signs at the cardiac apex which suggest mitral-valve obstruction when such does not exist. Occasional cases of extensive external pericardial adhesions resulting in a large heart and signs at the apex suggesting mitral obstruction have been described, although I have not personally observed such. On the other hand we occasionally

see cases of well marked mitral obstruction which are difficult to recognize as such because certain other factors have altered the classic physical signs. The presence of auricular fibrillation modifies the crescendo character of the murmur. Furthermore, we have seen severe congestive failure associated with dilatation of the heart result in an obliteration of the previously crescendo character of the murmur, the crescendo character later returning as the heart tone improved. The same factor—dilatation—may weaken the slapping quality of the first heart sound which we should like to have present to be certain of serious mitral valve obstruction. In view of these possible modifying factors, did he have important stenosis of the mitral valve? If we could say for certain he did not have auricular fibrillation I should guess that the mitral lesion was not extensive. On the other hand we cannot be certain of that one point.

There are a few other studies which might have been of some help. It was not possible to study the case completely. How much would an electrocardiogram have helped? It would have been of interest to know whether he had as I suspect he did, predominantly left ventricular strain and hence, left axis deviation. To account for his paroxysmal pain it would have been helpful to see what evidence there was of serious coronary disease. In view of the nature of the structural defects present I think he may not have had such changes. If the electrocardiogram had shown intraventricular block, however, it would have been another point in favor of serious coronary disease. Then, if this were not auricular fibrillation a long P-R interval might have been suggestive either of a digitalis effect or, more probably, of an active process in his heart, of which we have no real evidence from the clinical course.

How much would an x-ray film have helped? It might have been of some aid in determining the shape of the heart with special reference to the left auricle and pulmonary conus. I should have been much more interested, however, in seeing if we could have demonstrated calcification at the aortic orifice or possibly at the mitral orifice. Finally, it would have been of some interest to have known what the Hinton reaction was, although I think we need not seriously consider syphilis.

Would a blood culture have helped? Here is a person dying of valvular heart disease. We like to exclude by this means the possibility of a superimposed bacterial endocarditis. I see no real reason to entertain seriously the idea that a reactivation of rheumatic disease was responsible for his failure.

In concluding, I should like to predict, with reasonable certainty, that this patient had chronic and extensive valvular disease dating back probably to juvenile rheumatism with stenosis of the aortic valve of considerable degree, probably with calcification, and mitral stenosis and regurgitation of somewhat less extensive degree. We have no legitimate evidence from the record to suggest tricuspid valve disease except that from previous experience in other cases of such extensive valvular damage the chances are perhaps one in three in favor of slight, but I think here unimportant, scarring of the tricuspid valve. I should be very much surprised if he had either bacterial endocarditis or active rheumatic myocardial lesions. Finally, I should like to hazard a guess that in spite of the angina pectoris for over two years, plus the initial episode of severe pain five years before his death the later course and duration of the terminal heart failure for two and a half years suggest that the major coronary vessels, although possibly narrowed may have been adequate and that in this instance the symptoms of coronary insufficiency may have been due largely to a combination of other factors, such as obstruction at the orifice, a relatively low systolic blood pressure and probably a low pulse pressure, and the increased demand, because of the extensive mass of cardiac muscle, for more blood than was available. My diagnosis then is chronic rheumatic heart disease with aortic stenosis, possibly calcific, mitral regurgitation and stenosis, angina pectoris and congestive failure.

DR. PAUL D. WHITE. I agree with Dr. Bland. I put down as a last and questionable diagnosis, coronary sclerosis and narrowing superimposed. I think he is right in assuming that there is often only valvular disease to cause coronary insufficiency. Aortic stenosis with calcification is frequently attended by coronary insufficiency. The terminal complication, I suppose, was pulmonary infection or infarction, explaining the fever in the final stage. Death without complications in congestive failure is extremely rare.

DR. HOWARD B. SPRAU. Statistically this is one of those cases where one would not be surprised to find that a certain amount of the pericardium was adherent.

DR. BLAND. I should like to ask Dr. White if he has ever observed physical signs at the apex suggesting mitral disease in a large heart which were secondary to aortic stenosis alone—the Austin Flint phenomenon.

DR. WHITE. Murmurs at the cardiac apex may be mistaken for mitral murmurs when they are really transmitted aortic murmurs. I suspect that often an apical systolic murmur is due to aortic

fore his death and consisted of an attack of severe pain following unusual exertion, with radiation fairly characteristic of a coronary origin. It lasted only fifteen minutes. He was a little upset for the rest of the day, but must have made a fairly good recovery. I should first like to determine the nature of this initial episode. I believe that acute coronary insufficiency offers the best explanation in view of the radiation of pain to both arms and the relatively transient nature of the attack. Did he have a myocardial infarct at this time? Probably not, but rather a transient coronary insufficiency.

What else should we keep in mind? This episode occurred out of a clear sky, apparently during what probably constituted unusual exertion for him. Did this cause a small tear in the aortic intima and a dissecting aneurysm in the media? I think there are several points against that interpretation. First, the duration of the pain seems hardly adequate for a tear or dissection. The radiation of the pain to the arms is reasonably good evidence against such an occurrence, as is also the absence of hypertension. I think then that we can safely discard dissecting aneurysm of the aorta.

Other things may happen to the heart in the stress of unusual strain—a valve may rupture. So far as I know that is usually not a very painful event. It is manifested more by an acute disturbance of the circulation or by an abrupt change of the physical signs in the heart. This patient's subsequent course does not suggest such an occurrence. I think, then, that he did not rupture a valve and probably not a chorda tendineae.

For the next two and a half years he was troubled by substernal oppression clearly related to exertion. So far as one can tell from the description this clearly represents angina pectoris. It is interesting, however, that for the final two and a half years of his life this manifestation of coronary insufficiency was replaced by the signs and symptoms of serious myocardial weakness and failure. Prior to the appearance of general venous congestion, this progressive myocardial failure was manifested by signs of predominantly left ventricular weakness. So much for the clinical course extending over a period of five years.

The past history is of some importance, I believe. He apparently had had rheumatic fever. Ordinary growing pains in children are not associated with fever, nor do such patients find it necessary to remain in bed because of discomfort. It would have been of some academic interest if we had known what his physical signs were some ten years before the onset of his last illness. It seems unlikely that syphilis played any part. Although he had had a urethral discharge in the

past, the physical signs do not suggest syphilis. The course of his heart disease is not suggestive.

Then we come to the admission. He came to the hospital with chest pain, and died two days later. He was studied in the hospital. His heart was forceful apical in position. The disease (in the heart) will have to specify. He had auricular fibrillation of importance in appropriate disease present. The rhythm with extrasystoles whether that can be related to the dilation with a well marked almost certainly. I have a description of the heart in the past. Insofar as the physical signs relate to the heart he had all that was marked aortic stenosis with an obvious murmur heard over the aortic area. The characteristic type of murmur transmitted to the aortic second sound, and the second sound, and the level and pulse pressure. We have to accept this with caution because he died at the time they were

In addition to the heart, we obtain additional physical signs at the apex which suggest aortic valve disease. At first glance the apical murmurs alone suggest involvement of the mitral valve. The systolic murmur and the diastolic murmur in this area suggest years to be a little cautious about murmurs at the cardiac apex. A big heart, previous physical signs taken. We now know the conditions which may simulate cardiac damage following cardiac damage. It has been particularly difficult to find that free aortic regurgitation does not produce signs at the cardiac apex. Mitral-valve obstruction. Occasional cases of extracardiac adhesions resulting in a fixed apex suggesting mitral disease, although I have observed such. On the other

see cases of well-marked mitral obstruction which are difficult to recognize as such because certain other factors have altered the classic physical signs. The presence of auricular fibrillation modifies the crescendo character of the murmur. Furthermore, we have seen severe congestive failure associated with dilatation of the heart result in an obliteration of the previously crescendo character of the murmur, the crescendo character later returning as the heart tone improved. The same factor—dilatation—may weaken the slapping quality of the first heart sound which we should like to have present to be certain of senous mitral valve obstruction. In view of these possible modifying factors did he have important stenosis of the mitral valve? If we could say for certain he did not have auricular fibrillation, I should guess that the mitral lesion was not extensive. On the other hand we cannot be certain of that one point.

There are a few other studies which might have been of some help. It was not possible to study the case completely. How much would an electrocardiogram have helped? It would have been of interest to know whether he had as I suspect he did, predominantly left ventricular strain and, hence, left axis deviation. To account for his paroxysmal pain it would have been helpful to see what evidence there was of serious coronary disease. In view of the nature of the structural defects present I think he may not have had such changes. If the electrocardiogram had shown intraventricular block, however, it would have been another point in favor of serious coronary disease. Then, if this were not auricular fibrillation, a long P-R interval might have been suggestive either of a digitalis effect or, more probably, of an active process in his heart, of which we have no real evidence from the clinical course.

How much would an x-ray film have helped? It might have been of some aid in determining the shape of the heart with special reference to the left auricle and pulmonary conus. I should have been much more interested, however, in seeing if we could have demonstrated calcification at the aortic orifice or possibly at the mitral orifice. Finally, it would have been of some interest to have known what the Hinton reaction was, although I think we need not seriously consider syphilis.

Would a blood culture have helped? Here is a person dying of valvular heart disease. We like to exclude by this means the possibility of a superimposed bacterial endocarditis. I see no real reason to entertain seriously the idea that a reactivation of rheumatic disease was responsible for his failure.

In concluding, I should like to predict, with reasonable certainty that this patient had chronic and extensive valvular disease dating back probably to juvenile rheumatism, with stenosis of the aortic valve of considerable degree, probably with calcification, and mitral stenosis and regurgitation of somewhat less extensive degree. We have no legitimate evidence from the record to suggest tricuspid valve disease except that from previous experience in other cases of such extensive valvular damage the chances are perhaps one in three in favor of slight, but I think here unimportant, scarring of the tricuspid valve. I should be very much surprised if he had either bacterial endocarditis or active rheumatic myocardial lesions. Finally, I should like to hazard a guess that in spite of the angina pectoris for over two years, plus the initial episode of severe pain five years before his death, the later course and duration of the terminal heart failure for two and a half years suggest that the major coronary vessels, although possibly narrowed, may have been adequate and that in this instance the symptoms of coronary insufficiency may have been due largely to a combination of other factors, such as obstruction at the orifice, a relatively low systolic blood pressure and probably a low pulse pressure, and the increased demand because of the extensive mass of cardiac muscle, for more blood than was available. My diagnosis then is chronic rheumatic heart disease with aortic stenosis, possibly calcific, mitral regurgitation and stenosis, angina pectoris and congestive failure.

DR. PAUL D. WHITE. I agree with Dr. Bland. I put down as a last and questionable diagnosis, coronary sclerosis and narrowing, superimposed. I think he is right in assuming that there is often only valvular disease to cause coronary insufficiency. Aortic stenosis with calcification is frequently attended by coronary insufficiency. The terminal complication, I suppose, was pulmonary infection or infarction, explaining the fever in the final stage. Death without complications in congestive failure is extremely rare.

DR. HOWARD B. SPRAGUE. Statistically, this is one of those cases where one would not be surprised to find that a certain amount of the pericardium was adherent.

DR. BLAND. I should like to ask Dr. White if he has ever observed physical signs at the apex suggesting mitral disease in a large heart which were secondary to aortic stenosis alone—the Austin Flint phenomenon.

DR. WHITE. Murmurs at the cardiac apex may be mistaken for mitral murmurs when they are really transmitted aortic murmurs. I suspect that often an apical systolic murmur is due to aortic

stenosis, and sometimes an apical diastolic murmur may be transmitted from the aortic area

DR WILFRID J CONIEAU I should like to ask if it is not unusual in calcific aortic stenosis, the result of long-standing rheumatic heart disease, not to have an aortic diastolic murmur

DR BLAND Yes I was disappointed that there was not recorded at least a slight aortic diastolic murmur, provided that we are correct in assuming this aortic stenosis dated back to juvenile rheumatism

DR WHITE A good many cases that I have seen with marked aortic stenosis have had none The aortic valve openings of these cases become narrowed with age and the diastolic murmur decreases, as does the pulse pressure

DR BENJAMIN CASTLEMAN It is noted in the outpatient record that there was a harsh systolic murmur at the base, and a faint diastolic blow

DR BLAND That would be more in keeping with a rheumatic scarring of long standing

CLINICAL DIAGNOSES

Rheumatic heart disease with stenosis, mitral and aortic

Arteriosclerosis, aortic and coronary

DR BLAND'S DIAGNOSES

Chronic rheumatic heart disease

Aortic stenosis (probably calcific)

Mitral stenosis and insufficiency (probably slight)

Angina pectoris

Congestive failure

ANATOMICAL DIAGNOSES

Rheumatic heart disease

Aortic stenosis, calcific

Chronic endocarditis, mitral

Anasarca

Congenital anomaly horseshoe kidney

PATHOLOGICAL DISCUSSION

DR CASTLEMAN This man had a large heart, weighing 650 gm, due for the most part to a left ventricular hypertrophy produced by a calcific aortic stenosis He had marked aortic stenosis with calcareous deposits in the sinuses of Valsalva Without a clinical history and without examining the mitral valve it would be impossible to distinguish this lesion anatomically from the so-called senile calcareous aortic stenosis which ordinarily shows no correlation with a history or the anatomic stigmas of rheumatic fever The mitral valve, however, contained a slight, but without any question a definite, rheumatic lesion

The chordae tendineae were shortened and slightly thickened, although there was very little stenosis The valve measured 10.5 cm in circumference There can be little doubt, therefore, that the aortic lesion was also rheumatic in origin The tricuspid and pulmonary valves were normal The myocardium showed no evidence of active rheumatic fever He had all the signs of heart failure—marked congestion in the lungs, half a liter of fluid in the abdomen, a liter in the left pleural cavity, and half a liter in the right The liver showed a severe degree of congestion with central necrosis We could not find any cause for the fever or any sort of complication that might have produced it We thought he died from pure heart failure due to aortic stenosis The coronary arteries were practically normal, showing only a few atheromatous plaques That would coincide with Dr Bland's idea that the anginal symptoms were secondary to the aortic lesion

DR WHITE Some of these patients may die from coronary insufficiency due to marked aortic stenosis, without any actual coronary disease

DR CASTLEMAN Do you think, Dr White, that deposits of calcium in the sinuses of Valsalva, although at autopsy showing no impingement on the coronary mouths, might have produced obstruction during life as the heart moved around?

DR WHITE The only effect that I can imagine would be invasion of the underlying structure Once in a while there will be involvement of the bundle of His and its branches by a calcified mass at the base of the aortic valve, and such invasion might conceivably press against a coronary artery just distal to its mouth

CASE 25412

PRESENTATION OF CASE

A sixty-five-year-old American housewife entered the hospital complaining of dyspnea of twelve hours' duration

One month before entry the patient had had an attack of "laryngitis" which cleared in about two weeks but then recurred and made her unable to talk above a whisper For this she had been taking a cough medicine and a "tonic" For five or six nights before the present admission she had experienced nightly attacks of nocturnal dyspnea with sweating and fatigue At 4 a.m. on the day of admission she was awakened by severe dyspnea and sweating and felt extremely weak She complained of an aching pain in the left axilla and left arm about the elbow Dyspnea and sweating persisted until admission

She had had a thyroidectomy many years before entry, and a perineal repair two years be-

fore, a small parotid tumor had been removed one year before.

Physical examination revealed a well nourished, well-developed, orthopneic and dyspneic patient, appearing above her stated age, who looked sick and pale. Her hands were cold. There was an old thyroidectomy scar in the anterior inferior region of the neck. The fundi showed marked arteriovenous nicking. The mouth and tongue were dry. The heart was enlarged to the left. The apical impulse was felt 12.5 cm to the left of the sternal line in the fifth interspace. The sounds were of poor quality. The blood pressure was 100 systolic, 70 diastolic. The rhythm was regular. The neck veins were distended two thirds of the way up the neck. There were scattered crepitant rales throughout the upper chest bilaterally, with dullness and almost absent breath signs and many crepitant rales at both bases. The abdomen was large. Liver dullness extended from the fourth intercostal space to five fingerbreadths below the costal margin, the liver was not tender or hard. The patient spoke with a whisper.

The temperature was 98.6°F., the pulse 102, and the respirations 28. A few hours after admission the temperature had risen to 101.5°F.

The urine examination was negative except for the presence of a +++ albumin test, and many white blood cells and a rare trichomonas in the sediment. The blood revealed a red-cell count of 4,200,000 with a hemoglobin of 85 per cent, and a white-cell count of 12,000 with 87 per cent polymorphonuclears, the smear was essentially negative. The serum nonprotein nitrogen was 51 mg per 100 cc. A blood Hinton test was negative. The electrocardiogram showed a ventricular rate of 100, an auricular rate of 100 and normal rhythm with a PR interval of 0.15 sec and elevated ST intervals in Leads 1, 2 and 4, with high take-offs, the QRS complexes in Leads 1, 2 and 3 had low voltage, with evidence of left-axis deviation an upright R₄ was absent.

The patient ran a slightly swinging elevated temperature throughout her hospital stay. The temperature ranged from 99.3 to 101.8°F., with daily swings. The pulse ranged up to 120 for two or three days and then gradually fell to 110 where it remained more or less constant until death. Respirations ranged from 25 to 30 until the time of death when they had gradually risen to 35. A laryngologist noted a subacute inflammatory laryngitis, probably secondary to subacutely infected antrums. The thyroid gland was palpable, especially on the left, in spite of her previous operation for adenoma. Six days after admission the patient developed an audible pericardial friction sound. Basal rales in both lungs

persisted. On the sixteenth day she suddenly became weaker. The blood pressure was 110 systolic. The heart sounds became poor, with a gallop rhythm. The rub became less obvious. She was placed in a tent and given oxygen. The next day she began to sweat and develop signs of engorgement in the neck veins. On the twentieth day she suddenly became worse, developing further dyspnea. The blood pressure rose to 125 systolic, 90 diastolic. She was given Salyrgan and obtained a good diuresis. The electrocardiogram remained the same during her hospital stay. A few rales were heard in the anterior chest, and on the twenty fourth hospital day she died.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON. From the history we have a fairly clear implication that this patient was suffering from left ventricular failure. She apparently had attacks of nocturnal dyspnea, which came rather suddenly. She was awakened also by a sense of collapse, at least sweating and extreme weakness. She also had an attack of loss of voice which was attributed to laryngitis, and pain in the left arm. I think the hoarseness may be important although it may be true that she only had ordinary laryngitis that was not directly related to her illness. The fact that it cleared up is perhaps of significance and we are of course wondering whether there was something in the mediastinum causing interference with the laryngeal nerve. The pain in the left axilla and left arm is not very thoroughly described,—the record does not state whether it was rather constant or of short duration—but taken together with the other symptoms it is suggestive of some disease involving the coronary vessels, either disease of the vessels themselves or something else that was interfering with circulation through the coronaries, perhaps involving their mouths. From the story I should be looking for something that interfered with myocardial function especially involving the left ventricle and something that was interfering with coronary circulation. If we put in the hoarseness as an important factor I should be thinking of the possibility of syphilitic aortitis or of aneurysm. I do not believe we have to consider other types of mediastinal lesions.

We do not know whether thyroidectomy was done for thyrotoxicosis or because of an adenomatous goiter. It seems unlikely that it could account for the present illness. If there were recurrent thyrotoxicosis we should expect more symptoms to go with it. So far, there is no suggestion of hypothyroidism with resulting coronary disease. The perineal repair is unimportant. How

about the small parotid tumor? Some of the parotid tumors are malignant, and one might be trying to tie this story up with recurrent malignancy, unless there is more evidence later on, I am going to leave that alone.

The physical finding of arteriovenous nicking is considerably overdone, I think, in the wards and by medical men in general. Of course a patient of this age should have some change in the arteries, and one finds a reported arteriovenous nicking or hears people talk of it generally in those patients where you expect to find it and not in those where you do not expect to find it.

The physical examination certainly corroborates the impression of cardiac failure. What more does it tell us? The heart was considerably enlarged, and the suggestion is that it was enlarged to the left and not so much downward. The neck veins were distended, indicating that there was some stasis and some difficulty in venous return to the right auricle, which might be due to cardiac failure alone or could be caused by difficulty with the pulmonary circulation. We shall assume that the liver was large, but I do not know if we are correct in so doing. It could be due to congestive failure, and the signs in the bases could be caused by fluid secondary to congestion of the lungs. I shall go back for a minute to the upper chest, just to be sure, there were scattered crepitant rales throughout. That means moisture in the lungs, and does not necessarily mean there was any other disease in the chest. I want to be sure that there is no suggestion of a mass, because I am still bearing in mind the possibility of aneurysm.

The patient spoke with a whisper so that this laryngitis, so-called, had apparently been present since the onset. One other word about that—difficulty with the voice sometimes occurs in heart failure alone. I think it is more commonly noted in cases of severe mitral stenosis, this being explained by impingement by the dilated auricle on the recurrent laryngeal nerve where it hooks around the aorta. I am leaving it that this patient had heart failure, and we shall go on and see if we have further evidence of what type of disease the patient had.

A temperature rise in a patient with cardiac failure is not infrequently seen. One does not have to postulate because of temperature and rales in the chest that the patient has pneumonia.

There is nothing striking in the laboratory examinations. She was entitled to albumin as a result of renal congestion, and also to a few white cells. The trichomonas were unimportant. There was a slight leukocytosis which is hardly high enough to be significant in connection with the possibility of a recent coronary thrombosis, although

it is consistent with it. The nonprotein nitrogen was slightly elevated, a finding consistent with congestive failure of the kidney. A blood Hinton test was negative. This is important where we are considering the possibility of syphilitic disease of the aorta, because almost all these patients have a positive test. There is perhaps one reservation—sometimes in active syphilis the Hinton test is reported negative when the Wassermann is positive. If the serum is diluted, the Hinton test becomes very strongly positive. That is true, is it not?

DR TRACY B. MALLORY: Yes. It is a prozone phenomenon, such as you see in the Widal reaction, it is very unusual, however.

DR RICHARDSON: So the negative Hinton test is strong evidence against syphilitic disease.

I cannot talk about the electrocardiogram with any degree of assurity. It is certainly abnormal and does show a normal rhythm. The high take-off that is referred to is not infrequently seen in coronary disease. The low QRS complexes are also consistent with considerable myocardial degeneration, perhaps on the basis of coronary occlusion. I do not know enough about the electrocardiogram to rule out the possibility of pulmonary embolus. With the story in mind it seems as if that were rather an unlikely possibility.

"A laryngologist noted a subacute inflammatory laryngitis, probably secondary to subacutely infected antrums." That evidence certainly suggests that the hoarseness was not due to involvement of the recurrent laryngeal nerve, because the throat man should have noted some evidence of paralysis in the cord if such were the case.

The thyroid gland was palpable, especially on the left and in spite of the previous operation for adenoma. I still do not believe that the recurrence of the thyroid tissue is important.

Of course one of the clinical signs of coronary thrombosis with infarction of the heart is a localized pericarditis over the area of infarction, as evidenced by a pericardial friction rub. The trouble is it is one of those things that you read about in the textbooks but are rarely fortunate enough to pick up. It usually comes nearer the third than the sixth day following infarction, but it is perfectly reasonable to assume in this case that we are dealing with infarction of the heart. We should not, however, forget the possibility of an acute pericarditis as a terminal event. From the physical signs there is no evidence that there is an accumulation of pericardial fluid, the heart sounds became poor, to be sure, but I think that they would have been looking for fluid and that we would have heard more about it if it had been present.

Why did the blood pressure rise? She became worse, and the blood pressure rose, that is a curious thing I do not know why it rose

"The electrocardiogram remained the same during her hospital stay That is a suggestive note because with recent infarction of the heart you frequently get no change in the electrocardiogram until sometime afterward

I have made out a case for coronary heart disease. Let me just consider for a moment whether I have gone too quickly to that possibility. Engorged neck veins are not the ordinary accompaniments of severe coronary thrombosis They may be present, however, in a case such as this where there is very marked congestive failure. I am not going to take the engorgement as evidence of a pulmonary embolus Of course a pulmonary embolus does produce engorged neck veins not infrequently, and it is one of the signs that are looked for As a practical matter however it is hard to use this sign in the differential diagnosis of pulmonary embolus and coronary thrombosis If you look over this story from the point of view of pulmonary embolus it is difficult to put the whole thing together I stopped here so long because we get caught so many times The pathologist quite frequently finds pulmonary embolism in patients from the medical wards when it has not been suspected, hence one should consider the possibility of pulmonary embolus in death from any cause However it does not seem probable to me in this case There may be incidental pulmonary infarction It is frequently present in coronary disease, but I shall stick to the thought that this patient had heart disease, primarily coronary, with coronary sclerosis and with a coronary thrombosis which should be fairly recent in spite of the fact that the electrocardiogram showed no change during her stay in the hospital I think there will be evidence of previous coronary attacks which have not appeared in the story I am assuming the voice change was due to laryngitis I do not believe there will be anything more in the lungs than congestion with of course the possibility I have just mentioned of there being a terminal pulmonary infarct, and finally, there will be passive congestion of the liver and kidneys. I do not believe this picture can be explained on the basis of primary pericarditis without other involvement and I shall not attempt to place the coronary thrombosis Are there any suggestions?

A PHYSICIAN When she became worse and again began to sweat and to develop signs of venous engorgement, could that indicate the beginning of a pericardial effusion?

DR. RICHARDSON You mean cardiac tamponade?

A PHYSICIAN Yes

DR. RICHARDSON It could be. On the other hand you would think there would be more evidence of pericardial fluid They do not mention any evidence of Ewart's sign or consolidation behind the left scapula There is no note in regard to increasing enlargement of the heart, and there was apparently no evidence of edema Most of the failure was left sided, although of course there must have been some right sided failure too to account for the enlarged liver and the engorged neck veins On the whole, though, I do not believe we can accept a diagnosis of cardiac tamponade.

A PHYSICIAN She became worse on the twelfth day, with a rise in blood pressure. Could you explain that on the basis of pulmonary embolism?

DR. RICHARDSON You ordinarily do not get a rise in blood pressure following pulmonary embolism but rather, a fall I am putting down the rise in blood pressure as one of those things I cannot explain

CLINICAL DIAGNOSES

Coronary heart disease, with coronary thrombosis
Congestive heart failure.
Pulmonary emboli

DR. RICHARDSON'S DIAGNOSES

Coronary heart disease.
Coronary sclerosis
Coronary thrombosis
Congestive heart failure
Small pulmonary infarcts?
Chronic congestion of lungs, liver and kidneys

ANATOMICAL DIAGNOSES

Coronary thrombosis, left descending branch.
Cardiac infarct
Cardiac aneurysm
Pericarditis, acute fibrinous.
Pulmonary infarcts, right lower
Pulmonary embolism?
Hydrothorax, bilateral
Ascites
Passive congestion of lungs, liver, stomach and duodenum
Cholelithiasis
Cholecystitis, chronic.
Duodenal ulcers acute.
Polyp of colon
Endometrial polyp of uterus
Fibromas of ovaries

Follicular cysts of ovaries
 Carcinoma of bladder, papillary
 Operative scar thyroidectomy

PATHOLOGICAL DISCUSSION

DR MALLORY She showed a very big heart which was both dilated and hypertrophied. It weighed 675 gm. The dilatation was mostly in the left ventricle and was rather unusual in character because it was restricted to a portion of the left ventricle near the apex. There was a localized swelling about 7 cm in diameter that bulged out from the surface of the heart, such a lesion is often called a cardiac aneurysm. The myocardium over this aneurysm was totally necrotic. In other words this was a fairly recent infarct with such marked weakening of the muscle wall that the ventricle had bulged out to form an aneurysm. The left descending coronary showed marked atherosclerosis and a fairly fresh thrombus, about 5 cm from the orifice. The circumflex branch of the left artery was markedly sclerotic, with the lumen narrowed to pinpoint diameter in several spots but with no area of complete occlusion. We have become more conscious of the fact in the past four or five years, particularly following the work of people like Saphir et al.¹ and Schlesinger,² that cardiac infarcts rarely result from occlusion of a single coronary artery. Almost invariably you will find multiple coronary lesions. A single coronary thrombus is generally quite well taken care of by the development of a collateral circulation, and it is only when other vessels in the heart are markedly diseased that the process proceeds to infarct formation. The pericardium showed a fibrinous exudate which was fairly diffuse, not merely limited to the area of infarction but covering the entire heart. It was not very extensive, however, and I do not believe there was any question of cardiac tamponade.

As is often the case in anyone over sixty-five, there were a great many other pathologic lesions which you could not connect up with the clinical symptomatology. She had, for instance, two acute duodenal ulcers, a polyp of the large bowel and a small papillary carcinoma of the bladder. The thyroid gland showed no particular evidence that anything had ever been removed. There were two lobes present, both of which had the large, diffuse, smooth appearance of colloid goiter. What had been taken out, I do not know, but she had

the scar of a thyroid operation. There were two small frank infarcts in the lower lobe of the right lung, and there was a large silent stone in the gall bladder. There were also bilateral ovarian fibromas, one of which was 4 cm in diameter and the other nearly 6 cm.

A PHYSICIAN Was there any fluid in the abdomen?

DR MALLORY About 500 cc. There was 400 cc in the right chest, and 200 cc in the left. Probably all those figures are below diagnosable amounts.

Cardiac aneurysms are virtually impossible to diagnose unless one has the good fortune to get an extremely good x-ray plate, then it is occasionally possible for the roentgenologist to pick them up. The only possible way in which they might be recognized clinically would be from their sudden rupture. They often do rupture, following which there is a filling of the pericardium with blood and death from cardiac tamponade.

A PHYSICIAN Could the aneurysm possibly account for the peculiar shape of the heart that they got clinically?

DR MALLORY I think it might have. We have no note in the autopsy record as to the angle of the heart, and I do not know how high the diaphragm was during life.

A PHYSICIAN I notice that the nonprotein nitrogen at admission was 51 mg per 100 cc, the assumption is that it stayed high. How much of the fibrinous exudate could be due to that?

DR MALLORY We do not get excited about a nonprotein nitrogen of 40 or 50 mg with nothing else to go with it. If she had had simultaneously a marked hypertension and a nonprotein nitrogen of 70 mg or over, then you would begin to think about uremia.

DR RICHARDSON It is difficult in these cases with heart failure, where you suspect the possibility of added renal failure, to separate the two. It is certainly true in the words that you may get a nonprotein nitrogen of 70 mg with heart failure alone. The usual way to handle such a case is to treat the heart failure, if the renal symptoms subsequently become more marked, it is usually safe to make a diagnosis of renal failure.

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The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

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PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
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MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway Boston, Mass.

SOCIAL HYGIENE ACTIVITIES IN ENGLAND

At the annual meeting of the British Social Hygiene Council in July, 1938, the annual report* was presented. This included a summation of the activities of its far-flung branches in various parts of the British Empire. The Council has for its aims the strengthening of the family as the basic social unit, the preservation of the quality of future generations, the promotion of high and equal standards of sex conduct in men and women, the prevention of and attack on genitoinfectious diseases and commercialized vice, and the co-ordination of various organizations interested in these objects. Its educational work has been effective. Syphilis has been cut down 50 per cent but is

still an important public health problem. Emphasis is placed on the need for the establishment of effective social service work in the provinces and rural districts in order to contact the large number of untreated cases and also the numerous defaulters from treatment. The need of "almoners" or trained social workers, male as well as female, is pointed out as a prerequisite for the success of any campaign against these diseases. The Council is carrying out a large amount of educational work among adolescents and is particularly concerned with the conditions in rural areas in close proximity to training camps.

Not only has syphilis been reduced but the reported figures show that men with early syphilis tend to report earlier than formerly and that there has been a definite increase in the number attending the treatment centers on their suspicion of having contracted a genitoinfectious disease. The cases of congenital syphilis under one year have shown an encouraging decrease, in spite of an increasingly careful watch for them. In the last ten years, deaths from both paresis and tabes have dropped considerably. Other encouraging features are the marked increase in serological tests in the last five years and the jump in spinal fluid examinations in the last two years, indicating the development of an increased index of suspicion in hospitals and among physicians.

In contrast with the data about syphilis the cases of gonorrhea show an increase in the last two years, perhaps because of a tendency to make greater use of the treatment centers.

This report brings notes of encouragement and advice to this country—encouragement in what may be expected to be achieved, and advice with regard to the value of education among adolescents and the need of social service work as parts of the medical attack on genitoinfectious diseases.

THE MEDICAL PRESS AND CIRCULAR 1839-1939

RARELY does the opportunity come for one centenarian to extend congratulations to another. The *Medical Press and Circular* formerly published in Dublin, now in London, has completed its hun-

Twenty-Third Annual Report of the British Social Hygiene Council (Interpreted), 119 pp. London: The British Social Hygiene Council (Incorporated), 1938.

dredth year of life, and the *New England Journal of Medicine* offers its sincere felicitations to this weekly journal, so long an important factor in upholding the best traditions of the medical profession in Ireland. The *Lancet*, of London, is also over one hundred years of age. These two weekly publications and, we trust, our own journal have played a not inconsiderable part in the maintenance and propagation of national traditions in Ireland, England and America.

The *Medical Press and Circular* in its early days was largely a journal of medicopolitical flavor, for it never intended to be a journal of a scientific nature given over to original contributions to medicine. It was then, and has continued to be, a medical news sheet with educational material concerning the general advances in medicine. More recently, there has appeared in this journal an important series of historical contributions, particularly the "British Masters of Medicine" series, later edited in book form by Sir D'Arcy Power.

In honor of the hundredth anniversary of the *Medical Press and Circular*, Dr. Robert J. Rowlette* has issued a book giving the history of the journal, with comments on its character and the men who have been associated with it. The volume is a fitting tribute to a medical publication which has always been devoted to the interests of the general practitioner. May the next hundred years' publication of this journal be as useful to the medical profession as it has been in the past!

*Rowlette, R. J. *The Medical Press and Circular* 127 pp. London: The Medical Press and Circular, 1939.

MASSACHUSETTS MEDICAL SOCIETY

NEW ENGLAND POSTGRADUATE ASSEMBLY

Sir Thomas Lewis has been obliged to cancel his visit to the United States, and his place on the program of the New England Postgraduate Assembly will be taken by Dr. Lewis A. Conner, professor of clinical medicine, Cornell University Medical College, New York City, consulting physician to New York, Bellevue and Memorial hospitals.

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

SEPTIC ABORTION, FOLLOWED BY PELVIC ABSCESS AND DEATH

Mrs. H. F., a twenty-three-year-old para IV, entered the hospital July 9, 1911. The patient had been flowing for three days; she at first stated that this was a regular period but later admitted that having gone several days past her expected date of menstruation she had introduced a catheter into the uterus. She had had chills and fever.

No family history was given. The patient's past history was uneventful. She had had two full-term normal deliveries, and one miscarriage four years previously for which she had undergone a curettage.

Physical examination showed a fairly well-developed woman with flushed face and parched lips. The tongue was dry. The temperature was 104.4°F, and the pulse 120. The heart sounds were clear, and the action regular; there were no murmurs. The lungs were clear. The abdomen was tympanitic throughout and soft but very tender in the lower quadrants. On vaginal examination the uterus was found to be retroverted and slightly enlarged. There was an indistinct mass on the left. The right vault was clear.

The blood showed a white-cell count of 23,000. The urine was cloudy, with a specific gravity of 1.024, and contained the slightest possible trace of albumin and no sugar. The sediment showed a few pus cells but no casts.

Without ether anesthesia, the uterine cavity was found to be 9 cm. deep; a small amount of debris was removed by the finger and a culture was taken, which later showed no growth. An intra-uterine douche of salt solution was then given, following which the uterus was packed with gauze saturated with tincture of iodine. This was left in place for two hours.

The temperature gradually dropped to normal, although the pulse remained elevated. On the fourth day the temperature rose very slightly, but the abdomen became markedly distended and tender. Vaginal examination showed fullness and tenderness in both vaults. The white-cell count had dropped to 12,000.

Under ether anesthesia, a median suprapubic incision was made and a large walled-off pelvic abscess was evacuated. A culture taken from the

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

pus showed streptococci. Drains were placed in both sides of the pelvis and the abdomen closed.

The patient seemed improved following operation. There was free drainage, and the original wicks were removed on the sixth day. On the seventh day another cavity was broken into through the abdominal wound, with the escape of a considerable amount of pus. The patient appeared to be doing well. The temperature remained normal, although the pulse stayed at about 120. On the tenth day following the abdominal incision and drainage, a vaginal examination was made, and as there appeared to be some bulging in the vaginal vault, it was decided to secure freer drainage by colpotomy.

Under ether anesthesia an incision was made in the posterior cul-de sac and through and-through drainage was secured by passing a tube from the vaginal incision up through the abdominal sinus. There was considerable bleeding and a gauze pack was inserted alongside the drainage tube in order to control it.

The gauze pack was removed the following day and this was followed by considerable bleeding. The patient was then etherized and the sinus repacked. The pulse at that time was 150. A subpectoral saline infusion was given. Two hours later the patient became pulseless. The dressing was taken down, but there was no bleeding. The abdominal drain was saturated with a 1:1000 solution of adrenalin, which was poured into the wound. Caffeine sodium benzoate, strychnine and intravenous salt solution were given.

The patient improved but the temperature began to rise gradually and the pulse rate remained elevated. A fecal fistula developed. Three days later, the wound in the bowel was enlarged and a Mixer tube introduced into the bowel. The patient's condition steadily grew worse. She developed an ulceration over the sacrum and finally died of exhaustion and chronic sepsis on the twenty-eighth day after admission.

Comment. The treatment of this case can be criticized from the beginning to the end. On entry the uterine cavity was found to be 9 cm. deep and although no instrumental curettage was done, an intrauterine douche of salt solution was given. Following this the uterus was packed with an iodine strip. The history does not state that the uterus was invaded because of bleeding or that the iodine strip was put in the uterine cavity to control hemorrhage. In the absence of this positive statement, it is probable that no hemorrhage existed. Entire conservatism would have done no harm. It is barely possible that the small amount of intrauterine treatment extended the infection.

Laparotomy was performed when the temperature ranged from 98.6 to 99.6°F and when the white-cell count had fallen to 12,000. The pelvic abscess, it is stated, was well walled off. Had this abscess been treated by colpotomy, if this were practicable, or entirely left alone until colpotomy were practicable, the infection probably would never have invaded the abdominal cavity. The second operation, that of colpotomy, was done on scant indication. Following this operation, the patient went steadily downhill.

Extended experience has shown that through and-through drainage in the pelvis is not successful, and that drainage should be established by vagina, if possible. Rarely is it ever advisable to open a pelvic abscess abdominally; results seldom, if ever, justify such a course.

RESOLUTION BY THE MIDDLESEX EAST DISTRICT MEDICAL SOCIETY ON THE DEATH OF CARL EDWIN ALLISON

WITHEAS, Dr. Carl Edwin Allison, our associate in the practice of medicine in this community for the past twenty years, has been removed by death, and

WHEREAS The members of the Middlesex East District Medical Society feel keenly the loss of one who was devoted to his patients, conscientious in all his professional relations and a loyal friend, and

WHEREAS We desire to extend our sympathy to his widow Mrs. Una M. Allison, and son, Burton Allison, therefore, be it

RESOLVED, That this resolution be entered upon our records and copies be sent to Dr. Allison's family and the *New England Journal of Medicine*.

IRA W. RICHARDSON, M.D.,
CHARLES E. MONTAGUE, M.D.,
FRANK T. WOODBURY, M.D.

DEATHS

BLENKHORN—JAMES BLENKHORN, M.D., of Stoneham, died October 8. He was in his seventy-sixth year.

Born in Nova Scotia, he received his degree from the New York University Medical College in 1893. He was a member of the Massachusetts Medical Society and the American Medical Association.

Dr. Blenkhorn was former town physician in Stoneham and had practiced there for thirty-five years.

His widow, two sons and a daughter survive him.

CASSIDY—JAMES M. CASSIDY, M.D., of West Springfield, died October 4. He was in his thirty-seventh year.

Dr. Cassidy received his degree from Georgetown University School of Medicine in 1919. He was a member of the Massachusetts Medical Society and the American Medical Association.

His nephew survives him.

CUSHING—HARVEY CUSHING, M.D., of New Haven, Connecticut, died October 7. He was in his seventy-first year.

Born in Cleveland, Ohio, the son and grandson of a physician, he attended Yale University and received his degree from the Harvard Medical School in 1895.

Immediately after graduating from medical school he was appointed house officer at the Massachusetts General Hospital. After two years in Boston, he went to Johns Hopkins Hospital and became an associate professor of surgery in 1903. In 1912 he was appointed Moseley Professor of Surgery at the Harvard Medical School and was chosen to head the surgical department of the Peter Bent Brigham Hospital. He retired in 1932 and the following year became the first Sterling Professor of Neurology at Yale University School of Medicine, a position which he held until his retirement two years ago.

Dr. Cushing was a fellow of the Massachusetts Medical Society and the American Medical Association. He held memberships in the American Surgical Association, American College of Surgeons, Society of Clinical Surgery, Society of Neurological Surgeons, New England Surgical Society, American Neurological Association, American Association of Neuropathologists, American Psychiatric Association, American Association of Pathologists and Bacteriologists, American Society for Experimental Pathology, American Academy of Arts and Sciences, National Academy of Science and American Philosophical Society. He was an honorary fellow of the Royal College of Surgeons, of London, Edinburgh and Ireland, and a foreign member of the Royal Society of London. In recognition of his various accomplishments and contributions he was the recipient of twenty honorary degrees from colleges and universities in this country and abroad.

His widow and four children survive him.

MISCELLANY

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The need of a hobby for those who lead a busy life is well recognized. This is particularly true of doctors, as so well expressed by Sir William Osler "By the neglect of the studies of the humanities the profession loses a very precious quality. Man does not live by bread alone. One cannot practise medicine early and late alone as so many of us have to do and hope to escape the malign influences of a routine life."

With this sentiment in mind and in view of the fact that music is a hobby, and "making music" a relaxation, the Boston Doctors' Symphony Orchestra was founded in March, 1939. The response to the first rehearsal was very enthusiastic, with an attendance of forty-five doctors from Boston and neighboring cities and towns. Progress was so rapid that a family concert, presented by seventy members, was given last June.

Continued development of the orchestra is hoped for this year. The officers have spared no effort in building a successful organization. To this end much more comfortable quarters have been obtained for rehearsals, and the officers are happy to announce that Alexander Theide, former concertmaster with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, and later, Jacobus Langendoen, outstanding conductor and composer and a member of the Boston Symphony Orchestra, are to direct the orchestra. Proposed plans include a public concert at the end of the season, the proceeds of which will be used for medical charitable purposes.

Rehearsals will begin on Thursday, October 19, at 8:30 p.m. and will continue every Thursday evening. Physicians, dentists and medical and dental students interested in music as a hobby are eligible for membership. Those who are interested should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEAcon 2430).

The officers for the coming year are as follows: president, Julius Loman, M.D., vice president, Martin Edwards, M.D., treasurer, Robert G. Vance, M.D., secretary, Welman Christie, M.D. The Council includes Arthur W. Allen, M.D., Alexander S. Begg, M.D., Hermann L. Blumgart, M.D., Milo C. Green, M.D., Robert M. Green, M.D., Roger I. Lee, M.D., W. Jason Mixter, M.D., Abraham Myerson, M.D., A. Warren Stearns, M.D. and Soma Weiss, M.D.

CORRESPONDENCE

COLLECTION AGENCIES

To the Editor I note that the Maine Medical Association has a Committee on Investigation of Collection Agencies. I believe the Massachusetts Medical Society should have a similar committee. In addition, since many of us have a large number of unpaid accounts, why should not the Society act as a whole and contact some agency or law firm to take charge of this angle. If said firm would compile a list of the poor payers for each district, which it should be able to do out of the commission it gets, it would help prevent us from extending credit to a large number of non payers, who make a habit of leaving one doctor as soon as he insists on some payment.

Incidentally there are a large number of men who have turned over accounts to one or another collection agency, only to find that the agency has taken not only a lion's share but practically the "whole hog." I know of several in this vicinity who have been so treated by one company, and I should be glad to hear from any others who have had a like experience. Perhaps if enough of us complained we could prevent such companies from doing business in this state, and we might even be able to get back from them some of the money owed us.

B. W. MANDELSTAM, M.D.

94 Broad Street,
Bridgewater, Massachusetts

NOTICES

ANNOUNCEMENT

ORA H. WAGMAN, M.D., announces the opening of an office at 28 Washington Avenue, Winthrop.

REMOVALS

ROBERT H. GOODWIN, M.D., announces the removal of his office to 84 Spring Street, New Bedford.

EGON E. KATTWINKEL, M.D., announces the removal of his office to 65 Sterling Street, West Newton.

SIGMUND FREUD MEMORIAL EXHIBIT

Dr. Sigmund Freud, father of psychoanalysis, died in London on September 23, 1939, in his eighty-third year. The Boston Medical Library, in conjunction with the Boston Psychoanalytical Institute and Dr. Isador H. Coriat, has arranged a memorial exhibit at the Boston Medical Library, 8 Fenway, Boston. The material on display consists of photographs, autographed letters, newspaper clippings, a bronze bust of Freud and first editions

of his works in German and English including complete sets of the collected works in German and English. The exhibition represents the very wide aspects of Freud's genius beginning with his early interests in organic neurology and his discovery of the anesthetic properties of cocaine. It shows the entire development of psychoanalysis, both in its medical aspect and in its applications to cultural problems.

The exhibition is open to the public and will continue until further notice.

BOSTON DISPENSARY

A luncheon meeting of the clinical staff of the Boston Dispensary will be held on Friday October 20 in the auditorium of the Joseph H. Pratt Diagnostic Hospital at 12 o'clock noon.

The program under the auspices of the genitourinary department, will begin at 12.30 p.m.

PROGRAM

Gonococcal Infection and the Genitourinary Clinic.
Dr Oscar F Cox.

Some Attempts Toward Understanding and Changing the Social and Personality Factors Which Obstruct Treatment In a Gonorrhea Clinic. Miss Helen B. Hooker

Anyone interested in the subject is cordially invited to attend.

ROBERT W. BUCK, M.D., *President*
JAMES M. BATT, M.D. *Secretary*

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide former concert master with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra two Thurs-

days at 8.30 p.m., beginning October 19 in Studio A Station WMEA, 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr Julius Loman Pelham Hall Hotel Brookline (BEA 2430)

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic of the Peter Bent Brigham Hospital will be held on Wednesday afternoon October 18 at 2-00. Drs. C. S. Burwell and H. F. Newton will speak on "Dyspnea." A clinicopathological conference, conducted by Dr Elliott C. Cutler will follow.

On Thursday morning October 19 at 8.30 there will be a combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER, M.D., *Secretary*

MASSACHUSETTS GENERAL HOSPITAL

The alumni of the Massachusetts General Hospital are invited to attend the following events scheduled for the morning of either Day Monday October 16.

PROGRAM

- 9-00 Surgical grand rounds. Amphitheater George Robert White Memorial Building
- 9-30 Neurological staff clinical conference. Ether Dome.
- 11-00 Medical grand rounds. Ether Dome.
- 12-00 Clinicopathological conference. Pathology Building
- 1-00 Luncheon to meet the trustees and staff Red Brick Corridor

N. W. FAXON, M.D. *Director*

CENTRAL MASSACHUSETTS ALUMNI CLUB OF BOSTON UNIVERSITY SCHOOL OF MEDICINE

The Central Massachusetts Alumni Club of the Boston University School of Medicine will hold its fall meeting on Wednesday October 18 at the Worcester State Hospital. The scientific program will begin at 8-00 p.m.

Dr Harold J. Jeghers will speak on 'Important Vitamin Deficiency Diseases' Their diagnosis and treatment.

Physicians are cordially invited to attend the scientific meeting

DONALD K. MCCLUSKY, M.D., *Secretary*

NEW ENGLAND PATHOLOGICAL SOCIETY

The first meeting of the New England Pathological Society for the 1939-1940 season will be held on Thursday October 19 at 8-00 p.m., on the roof of the Palmer Memorial Hospital 195 Pilgrim Road, Boston.

PROGRAM

The Effect of Radiation on the Blood. Dr Charles E. Dunlap

Fat Embolism. Dr Lorne M. Gray

The Significance of Chronic Mastitis as a Precancerous Lesion. Dr Shields Warren.

BENJAMIN CASTLEMAN, M.D. *Secretary*

NEW ENGLAND SOCIETY OF PSYCHIATRY

The semiannual meeting of the New England Society of Psychiatry will be held at the New Hampshire State Hospital Concord New Hampshire on Wednesday October 18

Luncheon will be served at 1-00 p.m., following which there will be a business meeting.

The speaker of the afternoon will be Dr Ross McC. Chapman, superintendent of the Sheppard and Enoch Pratt Hospital, Towson, Maryland, and former president of the American Psychiatric Association

NEW ENGLAND HEART ASSOCIATION

A special meeting of the New England Heart Association will be held at the Boston Medical Library on Monday evening October 30 at 8 15

Dr Harry E. Ungerleider and Mr James D. Ewing of the Equitable Life Assurance Society New York City will speak on "Insurance Frauds and Disability Problems in Heart Disease."

Interested physicians and medical students are cordially invited to attend.

EDWARD F. BLAND, M.D., *Secretary*

are several historical descriptions that are well written and of extreme interest—notably those on lymphopathia venerea and colostomy. Illustrations are extremely numerous and well prepared.

Those chapters dealing with cryptitis and papillitis, fissure, fistula and hemorrhoids are excellent and contain many important details of symptomatology and treatment. Frequent nice clinical observations, such as that of the "pain interval" in relation to fissure, are interspersed throughout the book. The discussion of pruritus ani, with its reference to over 100 articles in the literature, indicates the multiplicity of opinions and the lack of convincing evidence as to the etiology of this annoying and obstinate condition. Tuberculosis and venereal disease are treated with extreme adequacy, and the portion on lymphopathia venerea in its relation to stricture is especially worthy of comment. Tumors, benign and malignant, are also presented in great detail, and the various therapeutic measures, particularly those involving surgery, are given in remarkable completeness, with a careful attempt to evaluate the various procedures.

Proctitis is fairly well presented, but the various types of dysentery and ulcerative colitis appear to be discussed largely on the basis of the experience of others. Many important details are lacking or receive scant attention, due, no doubt, to the fact that they are presented from a strictly proctological and surgical point of view, with little real knowledge of the broader considerations necessary for a proper conception of the underlying morbid processes. Appendicectomy and medicated instillations are advocated as valuable therapeutic measures in the treatment of ulcerative colitis—measures that have largely been abandoned because of their inadequacy. Mucous colitis is similarly discussed, with many references to the literature, but with very little or no attempt at a careful appraisal of this important condition. Many traditional concepts, such as the role of various foodstuffs in causing anal or rectal irritation, are presented without any inquiry as to the value of such conceptions, and without any obvious reservations. A few considerations, such as the autonomic control of the internal sphincter, are incorrectly stated. Atropine derivatives, presumably to block the action of the parasympathetic nerves, and sympathectomy are both advocated for the treatment of spasm in Hirschsprung's disease.

In spite of certain inaccuracies, and the inclusion of some material that detracts from clarity, the volume represents a careful attempt on the part of one man to present a complete and authoritative treatise on those conditions affecting the anus, rectum and sigmoid. It should serve as an excellent book of reference.

The Surgery of Oral and Facial Diseases and Malformations Their diagnosis and treatment including plastic surgical reconstruction George Van Ingen Brown Fourth edition 778 pp Philadelphia Lea & Febiger, 1938 \$10.00

The author of this book is well known in medical and dental circles, and his book on the surgery of oral and facial diseases has been for years one of the standard textbooks of surgery. This fourth edition has been completely rewritten, and many new chapters added. The book consists of twenty-five chapters. It covers a very wide field dealing with diseases and deformities of the face, mouth and jaws. In a work of this kind there is likely to be more emphasis on some subjects than on others, and some omissions are naturally present. It is practically impossible to describe all the salient features in this book, but on the whole the author's presentation of

the subject matter is well adapted for dental and medical students.

The section on cleft palate is of great interest. After long years of experience the author has adopted a method of osteal uranoplasty as a most desirable procedure for closure of the palate. This is a method that is not universally adopted. Chapters on fractures of the facial bones are not so complete as one would expect in a work of this type. The same may be said of the sections dealing with the type of deformities of the jaws that are characterized by extensive retrusion or prognathism. However, in the reviewer's opinion, the book is a useful contribution and will be welcomed by teachers of oral surgery as well as by students.

Diseases of the Mouth and Their Treatment A textbook for practitioners and students of medicine and dentistry Hermann Prinz and Sigmund S Greenbaum Second edition 670 pp Philadelphia Lea & Febiger, 1939 \$9.00

The second edition of this book is a more comprehensive textbook of diseases of the oral cavity than the previous edition, and a new chapter on lymphadenitis has been added. Other additions include articles on Paget's disease, hereditary pseudohemophilia, sarcoidosis and numerous other conditions. A very acceptable classification of tumors of the mouth, with many new illustrations, portrays the respective neoplasms.

This book, written by a dermatologist and a dentist, approaches the ideal textbook for both medical and dental students and a reference book for the practitioner of medicine. The oral cavity has been a very much neglected field in medicine, and the curricula in medical schools do not cover much of the material which is found in this volume. As the oral cavity may be considered the "diagnostic mirror" of the body, there is hardly a specialty in medicine where knowledge of the diseases of the mouth is not needed to round out a knowledge of morbid processes.

The oral manifestations of various constitutional diseases, including metabolic disturbances, blood dyscrasias, avitaminoses, are considered, and diseases of the ductless glands are thoroughly discussed, with numerous references to the voluminous literature on these subjects. Furthermore, the oral manifestations in skin diseases, including pigmentation in drug eruptions, are presented in a very clear manner. The authors combine the viewpoint of the physician with that of the dentist and present the subject both as a medical and as a dental problem—as many of the oral diseases should be considered.

The book is well compiled, and illustrated with both photographs and colored drawings, it is the most complete textbook on stomatologic lesions available at the present time. The volume can be recommended to both the practitioner of medicine and of dentistry, and should serve as a valuable source of information in diagnostic problems.

Éléments de Physiologie Clinique de l'Appareil Circulatoire J Castaigne and P Dodel 146 pp Paris Masson et Cie, 1939 27 Fr fr

The authors present a brief resumé of the physiology of the heart and blood vessels. The material presented is covered by any comprehensive textbook of physiology. Nevertheless the presentation is of value because it is written from a clinical standpoint. A short but succinct bibliography is appended to each chapter.

The New England Journal of Medicine

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VOLUME 221

OCTOBER 19, 1939

NUMBER 16

NEW HAMPSHIRE MEDICAL SOCIETY

DIVERTICULA OF THE COLON*

LOUIS A. BUIE, MD†

ROCHESTER, MINNESOTA

DIVERTICULA are blind tubes or sacs branching from cavities or canals, and those which are found in the walls of the colon have been classified as true or false. In the former group have been placed those in which the wall of the pouch includes all the coats of the bowel. In the latter group are those diverticula in which the wall of the pouch is composed only of mucous membrane that has burst through the muscular layers and has projected itself beneath the serosal surface, which serves as the second covering. Just why the latter group of abnormalities should be considered false diverticula is not clear. Neither thinness of their walls nor the fact that they are thought to be acquired would seem to exclude them from the true diverticula.

Another classification is that in which diverticula are divided into congenital and acquired types. Although the issue has been somewhat clouded because of lack of explicit description, it is generally understood that congenital diverticula are those which are anatomic anomalies and which form during the prenatal period of development. Acquired diverticula are admitted to be those which appear in postnatal life because of developmental defects or because of some weakness which exists in certain portions of the colon. For example, where the mesentery fails to cover the bowel, where blood vessels pierce the wall of the bowel and so forth. It is usually assumed that congenital diverticula have four coats and that those which are acquired have only two. This distinction is acceptable, but it cannot be said that it is satisfactory because it is likely that among diverticula considered to be congenital there may be some the wall of which does not include all four coats of the bowel and it is also possible that

the wall of an acquired diverticulum may include all four coats.

A SUGGESTED CLASSIFICATION

A satisfactory terminology is possible if others can be abandoned. However, if methods of terminology heretofore in common use are retained, the object of my suggestion will be defeated. The classification which I suggest is as follows:

Prenatal diverticula. These diverticula develop in utero and are of two types. Those of the first type form as true anomalies, and all walls of the colon are included in the walls of the sacs. Those of the second type are hernias of the mucous membrane between the developing muscular structures of the colonic wall. They lie beneath the serosa, and their walls therefore consist of mucous membrane and serosa.

Postnatal diverticula. These form after birth. They are hernias of the mucous membrane through or between muscular structures of the colonic wall. They lie beneath the serosa, and their walls accordingly consist of mucous membrane and serosa. Separation of postnatal diverticula into two types therefore depends not on their structure but on why and when they form. Postnatal diverticula of the first type form because the wall of the colon is weak between imperfectly encircling muscular structures; pressure and other physiologic processes within the colon are normal. These diverticula appear in adolescence. Postnatal diverticula of the second type form because pressure and other physiologic processes within the colon are sufficiently abnormal to force the mucous membrane of the colon through or between what would be presumed to be adequately encircling muscular structures. These diverticula appear in adult life, usually not until the fifth decade.

* Read in part before the annual meeting of the New Hampshire Medical Society, Manchester, June 8, 1939.
† From the Service on Proctology, The Mayo Clinic, Rochester, Minnesota.
(Precedence of proctology, The Mayo Foundation.)

ETIOLOGY

The causes of that small number of diverticula which can be considered prenatal and of those which can be considered as the first type of postnatal do not need further comment here. Those forces which are responsible for development of the second type of postnatal diverticula need further elucidation. So far, no one knows exactly why and how these pouches form and why they fail to appear before middle or old age, but it may be surmised that like hernias elsewhere in the body they come when age, with its attendant wear and tear and atrophy of tissues, has thinned the muscle fibers and separated them.

The colon is nourished by blood vessels which pierce its walls, and certain parts are weak where the mesentery is attached, nevertheless, diverticula probably will not develop at these points until further weakness appears with the changes which accompany advanced years. The increased pressure of gas which normally forms within the colon, or the strain of undue physical effort, may cause no irregularity early in life, but as gray hairs appear the colon becomes more susceptible to such influences and diverticula may be the result. Therefore, these anatomic irregularities may occur not only as a result of unusual strain and so forth, but also because of the effect of normal processes on tissues which have developed abnormal characteristics.

INCIDENCE

Anything simulating a fair appraisal of the frequency with which diverticula develop in the colon probably will never be made. No hint of their existence is ever given until they become the site of another pathologic process, and although it is impossible to determine the exact frequency with which this happens, it is likely that, in comparison with those cases in which dormant diverticula exist, the secondary pathologic development is of extremely rare occurrence. An individual may live his entire life harboring colonic diverticula, yet never become aware of their presence.

In the absence of more satisfactory methods of computing the incidence of diverticula of the colon, it has been necessary to rely on the experience of the pathologist in his routine post-mortem examinations, and on that of the roentgenologist who has examined the colons of those who have had symptoms referable to the colon. Obviously the pathologist has a better opportunity than the roentgenologist to find these abnormal pouches in the colons of those who have not suffered ill effects from them. In a report of W. J. Mayo,¹ it is stated that Robertson on the post-

mortem service at the Mayo Clinic, noted an incidence of diverticulosis of more than 5 per cent among persons who had died when past forty years of age. It was also learned from data of the roentgenologic service, where colonic roentgenograms were made for routine diagnostic purposes, that diverticula were present in the colons of nearly 6 per cent of the persons examined. Practically all the patients who had diverticula were more than forty years of age.

For purposes of comparison, Weber⁸ has reviewed the records of 52,411 patients on whom roentgenologic examinations of the colon have been made at the Mayo Clinic. Diverticula were found in examination of 3137, an incidence of 5.9 per cent. None of these figures have any value in determining the incidence of diverticula, except among those persons who consult physicians for investigation of the cause of some disability.

The incidence of diverticulitis is also very difficult to determine. In one group of patients who were studied for preparation of this article and who came to operation it was as follows: of 1549 patients with diverticula of the sigmoid examined at the Mayo Clinic from 1925 to 1935, 181 (11.6 per cent) required surgical treatment. A further review of the records proves that about half those who had diverticula complained at some time of symptoms which could be attributed to inflammatory or other activity in these deformities. Telling⁷ stated that 60 per cent of patients with colonic diverticula have symptoms, whereas Jones² wrote that in only 12 to 15 per cent of cases of diverticulosis does diverticulitis develop. Weber expressed the belief that in 15 to 20 per cent of those colons in which he was able to distinguish diverticula roentgenologically there was evidence of diverticulitis. Our experience at the clinic, in this regard, has proved that there are some cases in which there is clinical evidence of diverticulitis but roentgenologic changes are not manifest. The number of such cases is not known, however, because in many cases in which a clinical diagnosis of diverticulitis is made proof of the existence of the condition is lacking.

ANATOMIC SITUATION

Although diverticula may occur in all segments of the colon, the left half has been reported by all investigators to be the commonest site, and our experience at the Mayo Clinic confirms that of others. In fact we have found that in practically all cases in which colonic diverticula are found the sigmoid is invaded. Moreover, diverticulitis is seldom found elsewhere than in the sigmoid or immediately adjacent to it. This can be explained by the prevalence of diverticula in

the sigmoid, the fact that the lower part of the sigmoid and the upper part of the rectum often are not covered by the serosal coat and the fact that patients who have diverticulitis are usually constipated and hence the rectum is usually full. In such cases the full brunt of the pressure of muscular hyperactivity as well as that of accumulated gas is exerted in the segment immediately above the blocked outlet, and it is in that segment that the blowout is most likely to occur. The use of cathartics and of mechanical methods to stimulate evacuation adds to the burden. Either of these measures may be properly employed to assist those who have diverticulitis but their improper use is commoner and is productive of trouble.

Much has been said about those portions of the circumference of the bowel in which diverticula are likely to occur, but it is doubtful if the significance of the available conclusions is worthy of the amount of time which has been given to the subject. The noteworthy factor which appears to have been established in this regard is that the deformities are more prevalent in those areas where blood vessels pierce the wall of the bowel and along the mesenteric border. A more significant observation is that any portion of the lumen of the bowel is commonly broken through to form these pouches, with the exception of that part which is augmented by the longitudinal bands as they attach themselves to the serosal surface.

PATHOLOGY

The diverticula themselves present a constricted neck at the point where they traverse the wall of the bowel and a dilated body, which expands after the sac has passed beyond the wall of the bowel. The size of the aperture and that of the cavity of the pouch vary somewhat, although the average diameter of the former usually is about 1 to 3 mm. and that of the latter 4 to 8 mm. In unusual cases these limits are greatly exceeded. Associated with the diverticula in the sigmoid one occasionally can observe small shallow pit-like depressions which give the impression that while some force was producing diverticula in adjacent parts these pits, instead of actual herniations were formed. At other points the mucosa and submucosa may traverse spaces in the muscular layers. Sometimes the protrusion fails to break through the longitudinal layer but pushes it ahead and later the longitudinal layer may undergo disintegration from pressure atrophy. Thus is formed a diverticulum which with its two layers, has usually been designated as of the false type, but which is in every sense

a diverticulum and by no manner of reasoning can be termed anything else.

Those pathologic processes which attack diverticula of the colon are either inflammation or malignancy, and such changes rarely occur in any segment other than the region of the sigmoid.

The inflammatory disorder may develop as a result of an accumulation of feces within the diverticular sac. After this material dries out it may produce irritation of the mucosal lining of the pouch and consequently an inflammatory reaction. This may be the ordinary method of development of diverticulitis, but inflammation of the sigmoidal mucous membrane may spread into diverticula and produce the same result. Once the mucosal lining of the diverticulum becomes involved it begins to disintegrate, and ultimately ulcerous transformation may develop. These changes then extend to adjacent tissues and, as the wall of the bowel and the mesentery become involved, the products of inflammation encroach on the lumen of the bowel and, extending in the other direction, produce perisigmoiditis and mesenteritis. With increased edema and thickening, the neck of the diverticulum may become obstructed and the sac may become dilated until it ultimately ruptures. In most cases the inflammatory and hyperplastic changes produce thickening, which may become so extensive as to be palpable through the abdominal wall. With perforation, abscesses, encapsulated within the substance of the inflammatory mass, may form, or the diverticulum may adhere to other segments of the bowel, to the bladder or to other adjacent pelvic viscera and break through to form fistulas. Because of the slow process, sufficient time is usually provided for development of a protective wall of inflammatory and fibrous tissue.

Malignant changes may develop within the mucosal lining of diverticula, and because of their situation their presence may be obscured for a long time. Although the association of diverticulitis and carcinoma is infrequent, the latter condition should be suspected until it has been proved to be absent.

SYMPTOMS

Abdominal discomfort of some type is the most constant single evidence of pathologic involvement of diverticula of the colon and although it may appear in bizarre forms and situations, depending on the complicating factors associated it is generally most prominent in the left lower sector of the abdomen. There may be an acute pain similar to that of acute appendicitis. In some cases there is intermittent, piercing pain. In other cases the pain may be a dull boring discomfort which is

almost constant. Acute attacks may be accompanied by abdominal rigidity, nausea and vomiting, with tenderness following the attack. Constipation is present in more than half the cases, but in no sense can this be considered a symptom of the disease. Of course there is an obstructive phase which occasionally assumes the proportions of an emergency, and in such cases a distinct, palpable mass is usually in evidence. Incidentally such masses, when attributable to diverticulitis, are inclined to recede, at least partially, following the acute phase, and when this does not occur one should bear in mind the possible existence of a carcinoma.

In about a fourth of the cases of diverticulitis vesical symptoms are manifest, these irregularities are attributable either to adhesion between the diverticulum and the vesical wall or to actual perforation and the formation of a fistula.

DIAGNOSIS

Roentgenographic Examination

It may be said that roentgenology provides the most valuable single aid in establishing the diagnosis of diverticulitis and is almost the only means whereby undiseased diverticula can be discovered. The symptoms and physical evidence, both of which have been described, along with roentgenologic study, provide means of diagnosis which compare favorably with those modern methods of investigation employed in determining the nature of other disorders.

In the Department of Roentgenology of the Mayo Clinic, the outline of the colon after a barium enema has been observed roentgenoscopically instead of the barium meal's being employed, and by this method the diverticula are seen as rounded, pouch-like shadows along the contour of the bowel. With Weber's modification of the double-contrast technic of Fischer other characteristic signs are observed which increase the efficiency of the diagnosis. The inflammatory disease irritates the involved segment, and the resulting hypermotility varies with the intensity of the process. There may appear only sharp, serrated haustra, the involved segment of bowel may present a somewhat narrowed lumen, or extreme occlusion may be observed. These deformities may manifest themselves as a false filling defect, owing to spastic narrowing which may become so severe as to approach complete occlusion, or an actual filling deformity produced by infringement on the lumen of the bowel by formative inflammatory developments around its circumference. One who is inexperienced may be confused because of the similarity of these irregularities to those produced by carcinoma, but if it is borne in

mind that in inflammatory disease the involved segment of bowel is likely to be long and that the contours are concentric, whereas in cancer the outlines are sharply irregular and the involved segment is much shorter, much of the difficulty will be avoided.

Proctoscopic Examination

Until a few years ago this method of examination provided little of value for the diagnostician as he attempted to determine the presence or absence of superimposed pathologic states in colonic diverticula. However, experience has taught him much. Because practically all superimposed pathologic states which develop in these deformities occur in those which lie in the sigmoid, the distortion produced should in most cases be visible on proctoscopic examination. Hence a special effort has been made to discover the signs of diverticulitis that can be seen on proctoscopic examination, and five signs have been identified.

1 *Relative immobility of the bowel in a segment which is normally freely movable*. This bit of evidence alone is not sufficient to establish a diagnosis, but when coupled with other characteristic irregularities it forms strong supporting evidence. In all cases in which a patient has been found to have diverticulitis, great difficulty has been experienced in advancing the proctoscope its full length. There are other conditions, such as a short mesosigmoid, a fixed and retroverted uterus and pelvic inflammatory disease, which interfere with, or even prevent, complete proctoscopy, but these conditions also have features which aid in making the differential diagnosis.

2 *Angulation of the lumen of the bowel*. The physician may reach a certain distance with the proctoscope and find that the lumen turns sharply. This factor, along with immobility, may render further progress of the instrument very difficult or even impossible. In those cases in which we at the clinic have been able to insert the proctoscope farther we have observed additional features.

3 *Reduced lumen and mucosal folds*. This reduction of the lumen of the bowel is characteristic, and its appearance at once makes it clear that the contracture is owing to some influence which squeezes the wall of the bowel and produces the mucosal folds, as the lining membrane is crowded together. A little added pressure is often necessary in order to force the proctoscope ahead, and as this is accomplished it can be seen that the stricture smooths out somewhat and the folds of mucosa are partially obliterated. It should be stated that it is not always possible to complete this examination with a proctoscope of average

dimensions, and often, even when an instrument of much smaller caliber is employed, the examiner must admit defeat. In these cases, however, information is often gained which is sufficient to substantiate a diagnosis which until that time was only tentative.

4 *Sigmoidal sacculation* This peculiarity is normally observed in a mobile sigmoid which gives no evidence of perisigmoidal inflammatory disease, and usually, when it is discovered, if diverticula are seen on roentgenologic examination they are as likely to be dormant as they are to be producers of symptoms. The frequency with which diverticula are discovered in roentgenograms of patients who harbor them is striking. They appear as shallow pouches which may extend partially around the wall of the bowel or which involve its entire circumference, and they are separated by diaphragmatic or ridge-like elevations across the lumen of the bowel. These valve-like arrangements are elastic. They do not limit the lumen permanently or interfere materially with advance of the proctoscope, and they can be distinguished from spastic contracture by their failure to disappear.

5 *Seeing the diverticula* Whereas this is the most valuable single diagnostic sign it is rarely possible to see the diverticula in a case of active diverticulitis. Diverticula are seen most frequently when there is no associated inflammatory disease. They appear as small openings in the mucosa of the bowel, and offer one of the strongest arguments against the use of inflating devices during proctoscopy. The diameter of the lumen of these mucosal openings averages 2 to 3 mm., and often fecal concretions can be seen projecting from them.

One might suspect that some evidence of irritability or spastic activity would be observed in this condition but when it is realized that rarely is there any associated inflammatory disease of the sigmoidal mucous membrane absence of this evidence can be understood. The one important condition from which diverticulitis must be distinguished is malignant disease, and often there is no basis for suspicion that cancer is present except the finding of blood in the stool. This is because it is rarely possible to reach with the proctoscope the upper limit of the diseased portion of the bowel and whereas malignant features may not be observed in examination so far as it has been carried still it is not justifiable to report on the condition of the segment which has not been seen. When a patient gives a history of bleeding and it is impossible to find adequate reason for it the physician is justified in suggest-

ing the possibility of cancer. However, when hemorrhoids or other probable sources of blood are found, the value of the findings is greatly diminished and it can be reported only that cancer or hemorrhoids are present, or possibly both.

TREATMENT

Some investigators have been prone to regard inflammatory disease of diverticula as they have similar disease of the appendix, and forthwith have proceeded to treat the former as they treat the latter. They believe that with the appearance of acute symptoms surgical measures are immediately indicated. I think that a more conservative attitude should be observed. Sigmoidal diverticula do not swing free into the abdominal cavity as does the appendix, and experience has proved that rupture of diverticula, with resultant general peritonitis, rarely occurs. With periodic inflammatory attacks, these sacs become enmeshed in a hyperplastic mass of diseased and reparative tissues; this reduces the possibility of extension of the process to the abdominal cavity and renders formation of localized abscess more likely.

W J Mayo⁴ advised that when an abscess forms the pus be evacuated by incision instead of waiting for its spontaneous discharge, because the latter course may eventuate in fistula with its attendant evils. He expressed the belief that if more radical treatment should be indicated it could be postponed to a later and more favorable time, and recommended that if obstruction should develop colostomy be performed as close to the region of obstruction as convenient. In this manner, the stenosed portion can later be resected along with the colostomy opening through the same incision. Mayo also asserted that in some cases colostomy may be resorted to for temporary relief and the opening in the colon closed later if the infective process regresses spontaneously sufficiently to restore the lumen of the colon. With such a provision it may be possible to institute treatment with hot enemas or through and-through hot irrigations, with a catheter inserted in the distal segment of the bowel as a means of bringing about the recession more satisfactorily. Recently I have employed the Elliott treatment, using special applicators for the rectum but my experience thus far has been too limited to allow me to venture an opinion as to its value. In a former publication¹ it was advised that indications for surgical operation be considered to be acute perforation abscess, fistula (external vesical intestinal or multiple) inflammatory obstruction and cancer.

When none of these complicating circumstances

arise, medical management and treatment of a conservative type are preferable. Patients should be confined to bed and placed on a diet free from residue. Hot irrigations (110°F) should be used rectally. Ice bags should be applied to the left lower part of the abdomen. Often it will be found that acute symptoms are reduced in a short time, and after this a bland anticonstipation diet can be substituted. If there are any obstructive difficulties, mineral oil in small doses should be given, but if this feature is absent the oil need not be used. Antispasmodic drugs are of doubtful value. A patient should never cease to regard his problem seriously, and it will always be necessary for him to be careful about his diet and his intestinal

habits. In some cases he may avoid trouble permanently, but in other cases calamity may occur and require operative interference. If patients are so situated that skilled surgical attention is available, there is no reason why they should not care for themselves, under a physician's guidance.

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HYDATIDIFORM MOLE AND CHORIONEPITHELIOMA

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ALTHOUGH not a common condition, hydatidiform mole is sufficiently frequent so that most obstetricians encounter it occasionally. This pathologic entity is one in which the placenta is converted into a mass of grape-like bodies resembling hydatid cysts. These cysts, which vary greatly in size, represent a cystic degeneration of the stroma of the villi. In addition there is usually a marked proliferation of the epithelial layers of the villi. The danger from hydatidiform mole lies in its tendency to severe hemorrhage and its potential malignancy.

A group of 12 cases of hydatidiform mole in which hormone and pathological studies have been done has been investigated. In 2 of these the condition developed into malignant chorionepithelioma. This gives an incidence of 16 per cent, as compared with the generally accepted figure of 15 per cent. As usual, all the cases were admitted to the hospital from the second to sixth month of pregnancy. In only one third was the uterus sufficiently enlarged beyond its expected size to be clinically noticeable. All the patients entered the hospital because of bleeding, usually of several weeks' duration. In 2 cases the hemorrhage was so severe following the delivery of the mole that the uterus had to be packed and the patient transfused. There have been no deaths in this series, but 1 of the patients with chorionepithelioma is now in the hospital with pulmonary and brain metastases and the prognosis is hopeless.

The statement which is frequently made that signs of toxemia are often present in this condition did not seem to hold true in this series. Severe nausea with considerable vomiting was present in 5 of the cases. There was no case with a systolic blood pressure of over 120. Edema that was sufficiently marked to appear in either the history or

TABLE 1

CASE NO.	DURATION OF PREGNANCY mo	TOTAL URINARY PROLACTIN r u	FIRST NEGATIVE ASCHHEIM ZONDEK TEST wk
1	2½	200	2
2	4	25,000+ 25,000 (mole)	2
3	2	200	4
4	5	4,000	3
5	3	500 1,000 (mole)	2
6	6		2
7	3	1,000+	4
8	5	2,500 2,500 (mole)	3
9	3	25,000 (mole) 5,000 (corpus luteum)	2
10	5	200	2
11*	3	10,000+	6†
12*	3	500 (at operation)	None

*Chorionepithelioma
†After hysterectomy

the physical examination occurred in only 1 patient. The urine reports on the cases with catheter specimens were essentially negative. No other manifestations of toxemia were recorded. It is generally believed that there is an increase in the amount of urinary prolactin in this condition. We found this to be so in 7 cases, including one of the cases that became malignant (Table 1). The remaining 5 cases, including the

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other malignant one, showed a normal or low amount of prolan in the urine. There is a peak at about six weeks in normal pregnancy when large amounts of prolan are excreted. This production drops off very rapidly, and by the time moles develop a high value is abnormal. The amount found corresponds roughly to the amount of active trophoblastic cells in the placenta or mole. A mole with cystic villi and with slight trophoblastic proliferation gives a low titer while one with more trophoblastic tissue gives a higher one. The activity and amount of trophoblastic tissue is not necessarily related to its malignant potentialities. Some of the highest titers were obtained in moles that were benign, and one of the moles that became malignant had a very low titer. Once a mole has become malignant and invasion has begun, the hormone titer usually rises as the disease spreads. It is therefore extremely important that surgery be employed while the titer is still low.

While the commonest method in following these cases is the titration of prolan in the urine a study of the extracts of the mole and other tissues is of scientific interest. The amount of prolan recovered from the mole tissue corresponds very closely to that recovered in the urine. In one case a large amount of prolan, 5000 r.u. (rat units), was found in a corpus luteum cyst. In another case, which was seen only at autopsy and therefore is not included in this series, an extremely large amount of prolan, 10,000 r.u., was extracted from a lung metastasis.

From the clinical point of view it is extremely important to determine the onset of malignant invasion. Unfortunately, we are as yet unable to determine by microscopic sections of a mole whether it is potentially malignant. There are no histological criteria on which such a conclusion can be based. The amount of trophoblastic and syncytial proliferation, the number of mitoses and the maturity of cell types do not seem to answer the question and the sections of a mole that became malignant were called benign by several pathologists. The only definite proof of malignancy is the actual finding of invading fetal cells in the uterine wall and its blood vessels. This of course is impossible without a section obtained by hysterectomy. However, hormonal determinations may give a fairly accurate diagnosis.

In following the cases in this series, weekly Aschheim Zondek tests were done. Eight of the benign cases had a negative test at the end of two weeks after delivery of the mole. In 2 others the test was negative by the end of four weeks. Since there was no benign case which stayed positive over four weeks, it would seem that a positive test after a month is suggestive of malignant degeneration.

In the first of the 2 malignant cases the patient, a seventeen year-old white girl was three months pregnant by dates. Her uterus was the size of a five months pregnancy, and she had been staining for two months. A titration of her urine showed a large amount of prolan, 10,000 r.u. She was delivered of a large mole, following which Aschheim Zondek tests remained positive for six weeks. The test at this point showed only 166 r.u. of prolan. She was not bleeding but a diagnostic dilatation and curettage was done, which was negative. Because of her positive Aschheim Zondek tests a hysterectomy was performed. A solid, malignant chorionepithelioma about 3 cm. in diameter was found deep in the uterine wall and invading a large blood vessel. Six weeks following the operation the Aschheim Zondek test was negative. It is now two years since the operation, and negative tests have continued.

The other case of malignancy had been delivered three months previously of a hydatid mole at another hospital. When she appeared at our clinic she was staining. An Aschheim Zondek test showed 500 r.u. of prolan per liter of urine. Curettings were obtained that were diagnosed chorionepithelioma. A hysterectomy was done and a malignant tumor was found deeply invading the uterine wall and blood vessels. The Aschheim Zondek test has remained positive, and now, one year from operation, the patient is in the hospital with metastases in the lungs and brain.

The importance of early surgery is well shown by the two cases described. Any hope for the patient's recovery depends on removing the tumor at the earliest possible moment. The presence of a positive Aschheim Zondek test six weeks after the delivery of a mole is sufficient indication for surgery.

SUMMARY AND CONCLUSIONS

A study of 12 cases of hydatidiform mole has been carried out. Two cases developed chorion epitheliomas. Pathological study does not as yet give us definite criteria of potential malignancy in the mole. The urinary prolan is often high in this condition, but in some cases it is low. In all the benign moles the Aschheim Zondek test was negative within four weeks of the delivery of the mole. The presence of a positive test following this interval is suggestive of malignant degeneration.

It can be concluded that while a high urinary prolan may indicate a hydatidiform mole, a low prolan does not rule it out that all cases with benign moles should have a negative Aschheim Zondek test within four weeks after delivery and that a positive Aschheim Zondek test six weeks or longer after passage of a mole indicates the need for surgical intervention.

THE USE OF PAREDRIENE TO CORRECT THE FALL IN BLOOD PRESSURE DURING SPINAL ANESTHESIA*

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A MARKED fall in blood pressure is frequently encountered during spinal anesthesia. A variety of pressor drugs have been employed to correct or prevent this fall, including epinephrine, ephedrine,¹ Neosynephrin² and amphetamine (Benzedrine).³

Paredrine,[§] a drug recently introduced, has a powerful pressor action due to stimulation of the smooth muscle of the arterial wall,⁴ and is effective when given by mouth, intramuscularly or intravenously. Good pressor effects are obtained with 20 or 30 mg orally, 10 or 20 mg intramuscularly and 5 or 10 mg intravenously. These results suggested that the drug might be useful in correcting the fall in blood pressure observed during spinal anesthesia. The purpose of the present communication is to report the results obtained with Paredrine.

MATERIAL AND METHOD

Fifty patients in whom a rapid, marked fall in blood pressure occurred during spinal anesthesia were studied. All but 2 had abdominal operations, these exceptions had amputations of a lower limb. The drugs used to induce spinal anesthesia were novocain, in doses of 75 to 150 mg, and Nupercaine, in doses of 10 to 20 cc of a 1:1500 solution. In 5 cases (Table 1), 48 or 96 mg of ephedrine was given intramuscularly before the introduction of the anesthetic drugs into the subarachnoid space. Measurements of pulse rate and blood pressure were made every five minutes, when the latter fell markedly, Paredrine was administered in doses of 10 to 20 mg intramuscularly or 5 to 10 mg intravenously, or both. Measurements of the pulse and blood pressure were made every five minutes. The rise in blood pressure was considered satisfactory if the systolic pressure was maintained above 100.

RESULTS

In every case, the administration of Paredrine was followed by a return of blood pressure to a satisfactory level. The pressure usually began to

rise within five minutes after the intramuscular injection of 10 mg of the drug, if no rise was noted at this time, a second injection of the same dose was given. This invariably secured the desired result. The blood pressure was maintained

TABLE 1 Effect of Paredrine on Blood Pressure during Spinal Anesthesia

CASE NO.	DOSE	BLOOD PRESSURE BEFORE ANESTHESIA	BLOOD PRESSURE DURING ANESTHESIA	BLOOD PRESSURE AFTER PAREDRINE	DURATION OF SATISFACTORY EFFECT
	mg	mm	mm	mm	min
1	10 I.V.	155/85	70/40	150/80	20
2	8 I.V.*	140/80	70/50	200/100	50+
3	10+10 I.M.	105/60	60/40	100/60	45+
4	20 I.M.	120/60	80/50	210/100	70
	10 I.M.		60/40	160/80	90
5	10 I.M.	160/80	80/50	160/80	35+
6	10 I.M.	120/70	30/0	150/80	50
	20 I.M.		60/30	145/70	35+
7	10 I.M.	100/60	70/50	120/70	35
	5 I.V. 15 I.M.		60/40	120/60	60+
8	10 I.M.	100/60	65/40	120/85	55
	10 I.M.		80/50	120/80	55+
9	5 I.V. 10 I.M.	120/80	0	250/120	100+
10	10+10 I.M.	130/70	70/40	130/70	90
11	10 I.M.	110/70	70/40	140/40	125+
12	10 I.M.	110/60	50/30	120/70	60+
13	10 I.M.	130/80	60/40	160/60	60+
14	10 I.M.	110/70	40/10	120/60	80+
15	10 I.M.*	140/80	100/60	170/80	50+
16	10+10 I.M.	200/110	70/40	240/140	50+
17	10 I.M.*	125/100	50/0	165/80	85+
18	10 I.M.	100/60	40/0	100/60	30+
19	10+10 I.M.	120/60	80/50	115/70	55
20	10 I.M.	100/60	0	100/60	20+
21	10 I.M.	130/70	80/60	170/100	55+
22	10 I.M.	125/80	50/0	130/75	50+
23	10 I.M.	130/80	0	120/80	50+
24	10 I.M.	110/60	70/30	100/40	40+
25	10 I.M.	120/60	70/50	140/80	80+
26	10 I.M.	90/60	60/40	120/60	30+
27	10 I.M.	120/80	80/60	110/70	30+
28	5 I.V. 15 I.M.	100/60	0	100/60	35+
29	5 I.V. 15 I.M.	110/60	0	230/100	70+
30	10 I.M.	120/60	70/40	150/80	80+
31	10 I.M.	100/60	70/40	170/80	40+
32	10 I.M.	110/60	70/40	110/70	40+
33	10 I.M.*	120/70	60/40	120/70	40+
34	10 I.M.	120/60	50/20	160/70	30+
35	10 I.M.†	100/60	50/10	100/60	30
	10 I.M.		50/30	110/60	40+
36	10+10 I.M.	100/60	70/40	130/50	90
37	10 I.M.	140/60	90/50	140/60	50+
38	10 I.M.	100/40	70/40	150/85	60
39	10 I.M.	100/70	70/20	110/50	35+
40	10+10 I.M.	115/40	40/20	140/65	55+
41	10+10 I.M.	120/80	0	180/85	85+
42	10+10 I.M.	160/100	80/60	170/80	40+
43	10+10 I.M.	130/60	80/50	170/90	40+
44	10 I.M.	100/50	70/50	120/60	55+
45	10+10 I.M.	120/60	70/50	150/60	45+
46	10 I.M.	120/60	90/50	150/70	80+
47	10 I.M.	135/70	70/50	140/70	30+
48	10+10 I.M.	100/40	40/0	110/50	35+
49	5 I.V. 10 I.M.	120/70	0	140/70	65+
50	10 I.M.	120/70	80/40	125/65	30+

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This study was aided by a grant from Smith, Kline and French Laboratories, Philadelphia.

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§Paredrine available as the hydrobromide is *p*-hydroxy-*α*-methyl-phenyl-ethylamine hydrobromide. It was kindly supplied to us by Smith, Kline and French Laboratories, Philadelphia.

*Received 48 mg ephedrine intramuscularly before spinal anesthesia.
†Received 96 mg ephedrine intramuscularly before spinal anesthesia.

at a satisfactory level for half an hour to over two hours following the intramuscular administration of Paredrine. Following intravenous injection a rise in blood pressure was detectable in

two or three minutes and lasted from twenty to fifty minutes. There was no correlation between the response to the injection of the drug and the body weight, the dose of anesthetic or the level of anesthesia in the patient. Changes in pulse rate were variable usually a return occurred to levels obtaining before induction of spinal anesthesia irrespective of whether the fall in blood pressure resulting from the anesthesia was associated with tachycardia or with bradycardia.

No untoward symptoms were observed. In 5 cases in which the blood pressure fell in thirty to seventy minutes after the injection of Paredrine, a second injection was required to maintain the pressure at a satisfactory level until the operation had been completed.

DISCUSSION

The data clearly demonstrate the value of Paredrine in correcting the fall in blood pressure observed during spinal anesthesia. As a result of experience with the 50 cases here reported, the procedure for the use of the drug has been standardized as follows:

When the systolic pressure falls markedly but not below 50, 10 mg is given intramuscularly. If no rise occurs within five minutes, a second injection of 10 mg is given intramuscularly. If the systolic pressure falls below 50, 5 mg is given intravenously. When the systolic pressure has again fallen below 100, usually in fifteen or twenty minutes after intravenous injection 10 mg is given intramuscularly.

In addition to the above reported cases, Paredrine has been successfully used in 3 cases of marked fall in blood pressure due to novocain given subcutaneously and in 1 case with a fall in blood pressure due to Avertin anesthesia.

Paredrine has certain advantages over other pressor drugs heretofore used in correcting or preventing the fall in blood pressure during spinal anesthesia. Epinephrine has only a transitory pressor effect; moreover this drug causes a marked tachycardia and predisposes to the development of cardiac arrhythmias. Amphetamine (Benzedrine) has a marked stimulating effect on the cortical centers. Ephedrine has a similar though less marked, cortical action and, in addition may cause tachycardia. Paredrine does not cause the cerebral hyperactivity such as is seen following the administration of amphetamine or ephedrine. It also differs from epinephrine and ephedrine⁵ in

that it has little or no direct stimulating action on the heart, all or most of its action being peripheral.⁶ In normal subjects no change in the output of the heart occurs in association with the rise in blood pressure which follows the administration of Paredrine.⁶ Data bearing on the effect of the injection of Paredrine on cardiac output in patients during spinal anesthesia are not yet available; such data are essential for a complete understanding of the action of the drug.

Some anesthetists prefer to give pressor drugs before the induction of spinal anesthesia in order to prevent a fall in blood pressure. Paredrine, in 10-mg doses given intramuscularly, has been used in this manner in approximately a dozen cases thus far. In most of these it prevented a fall in blood pressure. In an occasional case it merely delayed it, a second injection of 10 mg of the drug was, however successful in restoring the blood pressure to normal.

The properties of Paredrine suggest that it might be useful in the treatment of various types of peripheral vasomotor collapse. The results in a relatively small number of cases have shown that the drug is a useful adjunct in the treatment of this condition. These and additional data will be the subject of a report at a later date.

SUMMARY AND CONCLUSIONS

Paredrine is useful in raising the blood pressure to satisfactory levels if it becomes unduly lowered by spinal anesthesia. The pulse rate is maintained at or returns to levels obtaining before the induction of spinal anesthesia. Paredrine has little or no direct effect on the heart; its direct action being apparently limited to the peripheral vessels. No untoward effects have been noted after its administration.

A satisfactory procedure in using the drug for correcting the fall in blood pressure associated with spinal anesthesia is outlined.

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ACUTE LUPUS ERYTHEMATOSUS DISSEMINATUS^{*}

Report of a Case

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WITHIN recent years a condition that has gone under a variety of names, one of which is lupus erythematosus disseminatus, has been brought to the attention of the medical profession. On reviewing this and allied problems it is apparent that closely related states may give rise to quite different symptoms and yet eventually prove to have a common underlying mechanism. The reasons for reporting this single case are first, that one clinical feature presented was unique and for a while made the condition appear rheumatic, and second, that we wish to record the effect of radiation of the ovaries.

As early as 1871 Kaposi¹ reported this condition. Gross² found 37 cases in 6000 autopsies, but in only 11 was he certain of the diagnosis. In 1923 and 1924, Libman and Sacks^{3, 4} described a syndrome in papers entitled "A Hitherto Undescribed Form of Valvular and Mural Endocarditis." In these reports they cited 23 cases. The essential features to which they called attention were non-bacterial endocarditis, white-centered petechiae, pericarditis, glomerulonephritis, the absence of Aschoff nodules, pleuropulmonary symptoms, a tendency to leukopenia, purpuric rashes, and eruptions of the face resembling acute lupus erythematosus. They emphasized the fact that occurrence of many of these findings was inconstant and was not uniform in the different cases. Our knowledge concerning this condition became more crystallized following the publication of papers by Baehr and his collaborators^{5, 6}. Since then it has been more commonly realized that we are dealing with a generalized disease, involving many of the internal organs of the body, during the course of which skin lesions appear on the face, and which almost invariably run a subacute or chronic but fatal course. In the more recent reports⁷⁻¹⁰ it would seem that some cases at least are included that probably do not belong to this group.

CASE REPORT

M. B. (Medical 52625), a 16-year-old girl, was born in Boston and had lived there all her life. She was a normal baby. As a child she had had whooping cough, measles and scarlet fever. Four years before entry to the

hospital she had had an undiagnosed illness, at which time she was bedridden for 6 weeks and had a temperature as high as 103°F. She was subject to head colds, and had always been rather pale and not quite so vigorous as many children. During the fall of 1937 she complained of occasional headaches, which were relieved by aspirin, and also stated that her right shoulder was somewhat stiff and sore. Her mother noticed that there was some swelling and tenderness of the left wrist. These symptoms were not persistent or very severe.

In January, 1938, the patient contracted a cold with some nasal obstruction, and had fever and generalized malaise. Soon afterward she developed pains and aches in various joints and parts of the body. The fever and feeling of malaise persisted and she was seen in consultation by one of us on February 17. At this time physical examination showed a well-developed and nourished girl. The temperature was 102°F, the respirations 30, and the pulse 20. No rash was discernible. The mouth, nose and throat were normal. There was some swelling and tenderness of the left wrist and fingers of the left hand. The heart rate was rapid, the rhythm was regular, and a precordial friction rub was heard over the base of the heart. There was dullness at the base of the lungs posteriorly, with evidence of a small amount of fluid in both pleural cavities. The abdomen was normal. Electrocardiograms showed normal tachycardia and an auriculoventricular interval of 0.24 sec. The white blood-cell count was 5300, the red-cell count 3,800,000, and the hemoglobin 75 per cent. The clinical course remained unaltered until March 1, when a rosyr red rash appeared on both cheeks and over the bridge of the nose.

The patient entered the Peter Bent Brigham Hospital on March 22, 1938. Physical examination at this time was essentially the same as previously described, with the exception of a butterfly erythematous lesion over both cheeks and the bridge of the nose. There were also some small macular, non-raised, erythematous spots on the palms of both hands. The patient continued to have a fever. X-ray films showed free fluid in the right pleural cavity. A thoracentesis was done, with the removal of 500 cc. of straw-colored fluid which was sterile on culture, the specific gravity was 1.010, and the cell count 1685 per cubic millimeter, with 1664 red cells. Blood Wassermann and Hinton tests were negative, the gonococcus complement fixation test was positive on two occasions. The urine showed a specific gravity of 1.011, a slight trace of albumin, 8 to 10 red blood cells and 13 to 18 white blood cells per high-power field and a few hyaline and granular casts. The red-blood-cell count was 4,100,000, and the white-cell count 5400. On the 4th, 7th and 9th hospital days x-ray treatments were given to the ovaries for the purpose of sterilization, the total dose was 1630 r. The day following her last treatment the patient felt better than at any time since the onset of her illness. The temperature, which had persistently remained at 103 or 104°F, dropped suddenly to almost normal. This improvement lasted for only 2 days. The patient developed a sore throat, and the temperature rose to 103°F, 2 or 3 days later she showed signs of pneumonia.

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of the right lower lobe and a Type 3 pneumococcus was recovered from the sputum. The nonprotein nitrogen of the blood was 30 mg. per 100 cc. and the total protein 4.3 gm. the albumin being 1.9 gm and the globulin 2.4 gm. From the time of admission there was a steady drop in the red-cell count to 2,740,000. The leukopenia persisted up to the time of the development of pneumonia at which time white-cell counts of 10,250 and 12,900 were obtained on successive days. The urine continued to show evidence of active nephritis. The course from this time on was steadily downhill despite sulfanilamide therapy. The patient became stuporous and anorectic, developed edema became markedly anemic and died on the 24th hospital day.

Autopsy The body was that of a well-developed and well-nourished girl. There was very slight café-au-lait pigmentation over the bridge of the nose and both cheeks.

The peritoneum was thicker than normal throughout. On its surface could be discerned many places in which boggy edematous fibrous tissue was found. Four hundred cubic centimeters of clear yellow fluid was removed from the peritoneal cavity. The spleen, which was large was almost entirely surrounded by thin delicate, edematous, fibrous adhesions, which were readily broken by running the hands around it. No petechial hemorrhages were seen over the serosal surfaces. There were many small areas of infarction in the spleen and microscopically there were organized thrombi in a few arterioles.

There was no free fluid within either pleural cavity. No evidence of emphysema or empyema could be found. Each lung was firmly adherent with readily broken fibrous adhesions to the parietal pleura. The lungs showed areas of bronchopneumonia culture from which showed a Type 3 pneumococcus.

Cultures from both mastoids yielded Type 3 pneumococci.

The pericardial cavity contained 250 cc. of clear brown fluid. The surfaces, both visceral and parietal were covered with abundant shaggy fibinous exudate. Externally the pericardium was adherent to the pleura on each side.

The heart weighed 410 gm. There was no evidence of tendons of any of the valves, which were thin, membranous, translucent and freely movable. They showed no abnormality except for the mitral valve, around the base of each cusp of which were numerous tiny yellowish-red vegetations which were moderately adherent to the endocardium. Cultures of these vegetations yielded no growth. Over the papillary muscles on the right ventricle were many vegetations similar to those seen on the mitral valve. Microscopically there was edema of the heart muscle. There were occasional foci of degeneration of muscle fibers around small thrombosed vessels. No Aschoff bodies were seen.

The surfaces of the kidneys were studded with small red areas measuring up to 3 mm. in diameter. Petechial hemorrhages were also seen within the parenchyma. Microscopically there was a very slight generalized hyaline thickening of the glomerular capillaries, suggesting the "wire loop" lesions of Baehr, Klemperer and Schiff.⁶ Some arterioles showed intimal thickening with fibrosis.

DISCUSSION

The case corresponds quite clearly from a clinical and pathological point of view, to what is now called lupus erythematosus disseminatus. The first point of interest is that throughout the course of the disease there was a distinct delay in auriculoventricular conduction (PR interval 0.24 to 0.26

seconds). Inasmuch as no digitalis had been given, this finding in the early course of the disease before the rash appeared led us to believe that the patient was suffering from rheumatic fever. In all previously published cases of lupus erythematosus, delay in auriculoventricular conduction was conspicuous by its absence.

The second point of interest was the attempt made to sterilize the patient as a therapeutic procedure. This was done because in our experience we have never seen a case of this type of lupus erythematosus in a man and because in all women the disease has occurred between puberty and the menopause. This sex relation has been clearly pointed out by Baehr.⁷ Although there may well be very rare cases in men, the fact of an overwhelming predominance of women during the menstruating period of life led us to institute sterilization by x-ray treatment of the ovary. It was believed that such procedure was warranted once the diagnosis is established since the outlook in this disease at present may be regarded as hopeless. It is of some interest that directly after the third x-ray treatment the temperature fell from 104 to 99°F in forty-eight hours. It was the first time in about four weeks that the temperature had been normal, moreover, the patient felt and looked better.

A short time after the subsidence of fever, an entirely different condition developed. She showed clinical evidence of lobar pneumonia, and a Type 3 pneumococcus was recovered from the sputum. Our belief that this was not a part of the underlying condition was supported by the development of leukocytosis, which had not been present during the previous six weeks. Although the illness terminated fatally, one is perhaps justified in further attempts at cure by sterilization, unless other curative measures are discovered in the future.

SUMMARY

A case of lupus erythematosus disseminatus is reported in which delayed auriculoventricular conduction was present. This led to an erroneous diagnosis of rheumatic fever in the early stages of the disease, before the rash appeared. X-ray treatment of the ovaries was instituted as a therapeutic procedure. The temperature quickly fell to normal with temporary clinical improvement, but this was promptly followed by a Type 3 pneumococcus pneumonia, which ended fatally.

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PAPERS FROM THE FAULKNER HOSPITAL

CASE RECORDS OF THE FAULKNER HOSPITAL

Antemortem and Postmortem Records as Used in Monthly Clinicopathological Conferences

Directed by J BEACH HAZARD, M D

CASE 6388

PRESENTATION OF CASE

A sixty-two-year-old American housewife was admitted with the complaints of nausea, vomiting and abdominal discomfort.

Three days before admission she became nauseated and shortly afterward vomited. At the same time she began to notice a vague discomfort around the umbilicus. In the evening, however, she felt better and was able to sleep well throughout the night. The following day nausea and vomiting recurred. There was no pain. Vomiting attacks persisted throughout the remainder of the time preceding entry. On the day the attacks began she had had two normal bowel movements but no others before admission.

Twenty-nine years before admission she had had an operation for extrauterine pregnancy. Two years before entry she had had a severe attack of nausea and vomiting with abdominal pain which disappeared in several days without treatment. She had avoided sweets because of bilious attacks, but she had not noticed any idiosyncrasies for fatty foods. The family history was noncontributory.

The temperature was 99.6°F, the pulse 88, and the respirations 22. The pressure was 164 systolic, 90 diastolic.

Physical examination revealed a well-nourished, co-operative woman in no apparent discomfort. The skin was sallow, and marked dehydration was apparent. The pupils were equal and reacted normally. Examination of the heart showed a regular rhythm and no murmurs. The lungs were normal. Examination of the abdomen showed no distention, no localized tenderness and no palpable masses. There was no tenderness in the costovertebral angles. The knee jerks were equal and active. A pelvic examination was not done.

The urine was of cloudy straw color and acid,

with a specific gravity of 1.019, and showed a slightest possible trace of albumin and no sugar, the sediment contained 10 to 20 erythrocytes and 1 to 5 leukocytes per high-power field and frequent finely granular and occasional hyaline casts. The blood showed a white-cell count of 13,800 with 73 percent polymorphonuclears, and a red-cell count of 4,800,000 with a hemoglobin of 87 per cent (Sahli). The icteric index was recorded as 25, but because of slight hemolysis of the specimen an accurate match was impossible.

Shortly after admission the patient felt some pain in the abdomen which was relieved by 1/6 gr of morphine. The afternoon of entry she vomited about 200 cc of dark-green fluid and soon after that 125 cc more. Throughout the day after admission, extreme nausea persisted and vomiting followed any attempt to take fluid by mouth. She complained of some pain in the abdomen. An enema was given with fairly good fecal results. Vomiting continued, and on the second night after admission the vomitus consisted of dark brown material with, at times, an extremely foul odor. X-ray examination of the abdomen showed marked dilatation of the loops of the small bowel. A faintly calcified area with a radiolucent center was present in the left side of the pelvis. A large ring-shaped area of calcification overlay the lower pole of the left kidney. The kidney outlines were of normal size and shape. The lumbar spine showed moderate hypertrophic changes.

An operation was performed on the third hospital day. The postoperative course was uneventful, and the patient was discharged on the eighteenth postoperative day.

DIFFERENTIAL DIAGNOSIS

DR HERBERT L JOHNSON. On physical examination at the time of admission this patient showed no distention, although the history suggests some type of intestinal obstruction. The absence of this sign is a significant fact and points

directly to a block high in the intestine. Low intestinal obstruction could not exist the number of days that this patient had been ill without some distention. The absence of localized tenderness is probably due to the fact the bowel was fairly well emptied by vomiting.

There is a history of an attack of nausea vomiting and abdominal discomfort two years previously which cleared in several days without treatment. This is consistent with high intestinal obstruction, which probably was relieved by the bowels being emptied by reverse peristalsis, with subsequent disappearance of obstruction.

Early in the onset of her second attack this patient had two bowel movements. She had no more until she had an enema in the hospital. In cases of obstruction I have noted the fact that it is difficult to convince patients with an acute block in the small bowel that they have obstruction. When one questions carefully it is found that there has been no diarrhea, but one or two fecal movements and a constant desire to defecate. Actually, the instant obstruction sets in there is this desire, and the patient often misleads himself and the family physician into thinking that the bowel is patent and that no obstruction is present. The fact that after several days she had a good result following an enema agrees with the picture we are trying to draw of high intestinal obstruction. The vomiting was apparently of fecal character and is in agreement with the above diagnosis.

Dilatation of the loops of small bowel on x-ray examination is corroboration of the assumption that this is small-bowel obstruction. The confusing part of the picture however is the following statement by the radiologist: "A faintly calcified area with a radiolucent center was present in the left side of the pelvis. A large ring shaped area of calcification overlay the lower pole of the left kidney. I assume that this means a ring of calcification with a dark center."

I think this woman probably had a high small bowel obstruction, but I cannot be sure as to what caused it. We must not overlook the fact that she had had a previous abdominal operation. It is possible that the calcified masses are related to blood clot or to placental tissue remaining after this previous illness. These masses may be calcified lymph nodes. That they are calcified masses within the bowel, however, is another possibility. It is difficult to be certain as to just what they are.

Any time that there is a story of a previous abdominal operation and of recent symptoms referable to the abdomen a relation existing between the two is of first consideration. Adhesions between the omentum and an old infected area or possibly a mass of clotted blood could afford a

site for either herniation or kinking of the small intestine. Adhesions could also be secondary to an infection present at or following her previous laparotomy.

It is my belief that this patient had high intestinal obstruction due, most likely to intraperitoneal adhesions.

DR. HENRY C. MARBLE: Did she have an intravenous pyelogram?

DR. MAGNUS I. SMEDAL: No, these were the only x-ray plates.

DR. MARBLE: Is that calcified area in the kidney pelvis?

DR. SMEDAL: It is exactly over the pole of the kidney.

DR. MARBLE: Why could not this be due to stones in the kidney? They could produce this entire picture.

DR. JOHNSON: The kidney outlines appear normal.

DR. MARBLE: She might have an acute hemorrhagic nephritis.

DR. J. BRANCH HAZARD: The urinary findings do not suggest such a diagnosis. A blood nonprotein nitrogen was not done, but could of course be high in the presence of intestinal obstruction.

We might ask Dr. Smedal his interpretation of the calcified masses.

DR. SMEDAL: I said that they were gallstones causing obstruction of the small bowel.

CLINICAL DIAGNOSIS

Intestinal obstruction due to gallstone

DR. JOHNSON'S DIAGNOSIS

High intestinal obstruction probably secondary to intraperitoneal adhesions

ANATOMICAL DIAGNOSIS

Gallstone (removed from small intestine)

PATHOLOGICAL DISCUSSION

DR. HAZARD: The findings in this case can best be given by Dr. Balch as my only specimen consisted of a gallstone measuring 3.9 by 3.2 by 2.9 cm and weighing 20.3 gr.

DR. FRANKLIN G. BALCH, JR.: This case was rather a puzzle to us when the patient first came in because she seemed in better condition than patients usually are with intestinal obstruction. This diagnosis, however, was our first consideration but we also considered gall-bladder disease that is why we watched her for a few days. Then with her clinical condition growing worse and with the x-ray findings we were convinced that the diagnosis of intestinal obstruction was cor-

rect On opening the abdomen we found multiple moderately distended coils of small bowel, with one loop reaching down to the pelvis In the left side of the abdomen we felt a mass, we pulled the loop of small bowel over into the operative field and removed a gallstone which is shown in the upper of these two shadows The body forming the lower shadow was never palpated

I might say that these cases are comparatively uncommon I looked up the cases at the Massachusetts General Hospital from 1898 to 1932, and only 10 occurred in some 500 cases of obstruction I should like to emphasize what Dr Johnson brought out, namely, that in the face of high obstruction a patient can have movements by rectum, because it is said that the bowels have moved does not exclude high intestinal obstruction, as was certainly the situation in this case

DR HAZARD At the time this patient was admitted we were gallstone conscious, two months previously a patient with symptoms of high intestinal obstruction had come to autopsy, which revealed a gallstone that obstructed the terminal ileum The way large gallstones get into the intestine is usually through a fistula between the duodenum and the gall bladder Gallstones have been reported up to about 10 cm in diameter

A PHYSICIAN What was the local condition in the bowel at the point of obstruction? Did it look as though the stone had been there for any length of time?

DR BALCH No, the bowel was in good condition I think the gallstone should be removed in most cases by backing it up and taking it out where the bowel has a wider lumen In this case, however, as the bowel was in good condition, we took it out where we found it, which I think was about at the junction of the jejunum and ileum

DR HAZARD Plates taken twelve days after operation showed an absence of both calcified masses, so that she must have passed the second stone

DR MARBLE Does Dr Balch think that the history of pain as given is accurate? "A very moderate amount of pain" is the only entry in the whole record Is this not a small amount of pain for an acute intestinal obstruction which is complete?

DR BALCH I do not believe that she had complete obstruction until shortly before the operation was performed I think the stone was coming down the intestine

DR MARBLE Would you not expect her to have more than "a very moderate amount of pain"?

DR BALCH Yes, provided she had a complete obstruction

DR MARBLE I thought obstruction and pain went hand in hand Apparently this woman had a painless obstruction

DR BALCH She had pain, but it was not severe

DR MARBLE I saw a patient the other day who had a kidney stone with obstruction She was vomiting and showed a clinical picture similar to that in this case Furthermore, last summer I saw a patient with obstipation and much more pain than this patient had Two days afterward he was found to have an acute hemorrhagic nephritis The intestinal symptoms were due to ileus associated with renal disease Considering the small amount of pain which this patient had, I still believe that kidney disease should be included in the differential diagnosis of the case

I also want to add that there is no note in this case that the patient had hyperactive audible peristalsis associated with the pain

CASE 6395

PRESENTATION OF CASE

A forty-seven-year-old, retired, American business man was admitted, with the complaint of pain in the right shoulder and chest

About five months before admission the patient developed an aching pain in his shoulder after shooting This seemed to be near the joint but was not aggravated by moving his arm He also noticed at this time that he tired easily About a month later, after he had been doing some heavy work, the soreness in his shoulder suddenly increased At this time he noted a slightly elevated temperature in the morning, which increased a degree or two in the afternoon This continued for a period of about four weeks X-ray films of the chest were taken and were said to show a lesion in the right apex He was sent to bed and had remained there constantly until admission The pain in the shoulder continued to grow worse and markedly disturbed his sleep Aspirin was given with no relief, but it resulted in profuse perspiration He occasionally had slight cough in the morning, which was unproductive. Coughing or sneezing resulted in some pain in the chest, which seemed to be partly in the muscles but for the most part inside the chest He was unable to lie on his right side The pain was of an aching character but was not very sharp and was most marked in the late afternoon and evening It was aggravated when he moved. Profuse night sweats occurred and were sufficient to require change of pajamas He had had a loss of appetite but had forced himself to eat He had also noted a marked loss of "pep" since being in bed and had not felt like getting up

There had been a weight loss of 30 pounds during the five months preceding entry.

About twenty five years before admission he had had dysentery but had recovered completely. He had had the usual childhood diseases. Many years before admission he had had an attack of "rheumatism" in his back and arms.

His father had died, probably of tuberculosis. His mother, wife and son were living and well. One grandfather and two aunts had had diabetes.

On admission his temperature was 99.6°F., the pulse 100, the respirations 21, and the blood pressure 140 systolic, 70 diastolic.

Physical examination revealed a suggestion of clubbing of the fingers. There was no atrophy of the intrinsic muscles of the hand. The pupils were slightly irregular in outline, of about equal size and reacted to light and accommodation. The eyegrounds were normal. Some teeth were missing, but those remaining were in satisfactory condition. The tongue was coated. There was no enlargement of the lymph nodes. The thyroid isthmus was palpable, but no nodules were noted. There was some limitation of motion of the right chest as compared with the left, especially in the apical region, examination of the chest was otherwise negative. The heart was not remarkable. The knee jerks were present, and the extremities were not remarkable. There was no limitation of motion in the upper shoulder girdle.

A urine examination showed a very rare leukocyte in the sediment. The blood had a white-cell count of 13,150 with 78 per cent polymorphonuclears, and a red-cell count was 3,700,000 with a hemoglobin of 75 per cent (Sahli). A stool examination was not remarkable. A blood Hinton test was negative.

X ray examination of the cervical and dorsal segments of spine the day after admission showed normal bone texture throughout. Stereoscopic films of the chest revealed a cloudy density occupying the entire right apex, with increased lung markings in the ascending bronchial branches. The remainder of the right lung field and the entire left lung field were normal except for several areas of calcification on each side. The diaphragmatic outlines were smooth, and both angles were clear.

On admission Sodium Amytal and phenacetin were administered for the pain in the right shoulder with some relief, but morphine was required to induce sleep. His temperature rose to 102°F. the night of admission and continued between 99 and 103°F., with a marked upward swing in the evening throughout his forty-three-day stay in the hospital. The pain persisted but was controlled by Sodium Amytal or chloral hydrate. His body weight on admission was 146 pounds and on the twenty-fourth day of his hospital stay was

138 pounds. Three blood cultures were negative. Two tuberculin (dilution 1:10,000) tests were negative. One sputum obtained on the second day after entry was negative for acid fast bacilli. A second chest film made twelve days after admission presented no change in the appearance of the right apex, but in addition a small patch of cloudy density was seen in the left apex, on reviewing the previous films the same area was found to be present. A flat film of the abdomen showed downward displacement of the gas-filled hepatic flexure and proximal transverse colon, apparently by an enlarged liver. Re-examination of the cervical and upper dorsal region of the spine was again negative. A gastrointestinal series performed sixteen days after entry was negative, as were films of the cranial sinuses and the skull. An oral Graham test performed twenty-two days after admission showed no filling of the gall bladder with the dye either before or after a fat meal and no evidence of opaque calculi. X ray films of the chest taken for bone detail showed numerous cavities in the area of increased density at the right top.

Because of a possible relation between the chronic cholecystitis suggested by Graham test and pain in the right shoulder, exploration was advised, and a cholecystectomy and exploratory laparotomy were performed about a month following entry. A culture of the gall bladder was negative. For a few days following operation, the pain in the shoulder disappeared but soon reappeared. The patient's temperature dropped almost to normal for a day or two but then rose. Agglutination tests for tularemia and undulant fever were negative. The patient's white-cell count varied during his stay from 13,000 to 16,500 and on discharge was 14,350 with the polymorphonuclears ranging from 63 to 75 per cent. The red-cell count varied from 3,400,000 to 4,000,000.

On the forty-third day after entry the patient was discharged home to the care of his family physician, with instructions to stay in bed for a while and to become ambulatory gradually.

Following discharge he continued to run a fever, gradually lost weight and strength and died approximately six months after leaving the hospital.

DIFFERENTIAL DIAGNOSIS

DR. THEODORE L. BADGER. The essentials in regard to this forty-seven-year-old man are that he was ill for nearly a year with fever and had pain in the right shoulder, loss of weight, fatigue, loss of appetite, unproductive cough and an x ray showing a lesion in the lung. Looking at the first x ray film taken in this hospital we find evidence of a healed primary tuberculosis, and in the right apex there is a definite flocculent infiltrate.

tion which has the appearance of an active tuberculous lesion. There seems to be no deformity of the chest, and no asymmetry. The trachea is in the midline. There is a little haziness of the left apex, but this is not of great importance. There was an early family history of tuberculosis.

On physical examination the only findings are slightly clubbed fingers. No mention is made of rales or other positive physical findings in the lungs.

His entire stay in the hospital was characterized by fever which ranged from 99 to 103°F, and I presume it continued until he died. The tuberculin test was negative in a dilution of 1:10,000. Any tuberculin test, however, should not be considered negative unless finally done in a 1:100 dilution of old tuberculin (OT) of known potency. It is possible that the long-continued fever had reduced his resistance and, hence, that he did not respond. Only one sputum analysis was reported, and it is a little difficult to know from that whether it was really negative. Gastric lavage under these circumstances would have been of importance, it is interesting how frequently acid-fast organisms are found in such material from patients whose sputums have previously been reported negative. Therefore we are at a loss to know whether there were tubercle bacilli present. The x-ray films show a progressive lesion at the right apex, with increased density of the markings at the hilus and at the apex of the lung. The cavitation shown in the Bucky plate has a honeycomb appearance.

During his stay in the hospital there was a weight loss of 10 pounds. A gall-bladder operation was performed, the only report given is that of a negative culture, and no note is made as to the character of the gall bladder or as to other findings that may have been present.

The final diagnosis of this case is open to some speculation. In regard to the possibility of its being tuberculosis, we have a history that the trouble started following trauma, namely shooting, and that not so long afterward he developed pain, cough and fever. Trauma can cause a quiescent tuberculous lesion to become active, and there are many such records. Blows on the chest and repeated shooting with a rifle or shotgun have been reported as a cause of reactivation. In this case the onset was somewhat insidious. The night sweats, persistent fever and unproductive cough are all consistent with tuberculosis. Physical examination was not particularly helpful, the only findings of interest being those of limited expansion of the chest. This x-ray film is quite in keeping with tuberculosis; however, I do not believe that any x-ray picture no matter how

much it looks like it, is typical of this disease. Tuberculosis can be simulated by a suppurative process and even by a fungous infection of the lung. Against tuberculosis we have the fact that the patient had a progressive apical lesion by x-ray, with little or no expectoration and no demonstrable tubercle bacilli.

A second possibility in diagnosis is that of carcinoma of the lung. There are several factors which indicate primary neoplasm of the lung rather than tuberculosis. Pain in tuberculosis is common, but in this case the constancy and the deep-seated, boring character of this symptom are indicative of a tumor. A loss in weight occurs with tuberculosis as well as with cancer, but such a marked loss as he showed favors the latter.

If we make a diagnosis of cancer, should we call it primary bronchiogenic or metastatic, and if the latter, where is the original focus? No mention is made as to what was found in the gall bladder. The relation between the pain in the shoulder and the gall bladder was pointed out, but I am inclined to believe that it is of little significance.

My final diagnosis in this case is cancer of a bronchus of the right upper lobe, with suppuration distal to the lesion. Chronic progressive pulmonary tuberculosis would seem most unlikely.

CLINICAL DIAGNOSIS

Tumor of right apex of lung

DR. BADGER'S DIAGNOSIS

Bronchiogenic carcinoma of right upper lobe of lung

PATHOLOGICAL DIAGNOSES

Poorly differentiated primary carcinoma of right apex of lung, with direct extension to adjacent ribs, intercostal muscles and vertebrae

Emphysema

Ascites

Myocardial fibrosis

Surgical absence of gall bladder

PATHOLOGICAL DISCUSSION

DR. J. BEACH HAZARD. As Dr. Badger has stated, the lesion in the apex of the lung was a primary carcinoma. There was no infection in the lung tissue but there was very extensive necrosis of the tumor in many portions and I think that might have caused the fever. There were several large emphysematous blebs in the vicinity of the tumor and they probably accounted for the area suggesting cavitation in the x-ray films. Distant

metastasis from the tumor had not occurred, there was, however, direct extension to the intercostal muscles and to the adjoining bone.

The gall bladder showed slight chronic inflammation in its wall but was otherwise negative.

This tumor belongs to the group of superior sulcus tumors to which attention has been called by Pancoast.* It is not the typical syndrome de

PANCOAST, H. K.: Superior pulmonary sulcus tumor; tumor characterized by pain, Horner's syndrome, destruction of bone androphy of lung muscles. J. A. M. A. 99:1391 1930 1932

scribed by him, however, as the cervical sympathetic chain was not involved, so as to cause a Horner's syndrome.

DR. EDWARD L. YOUNG Is the fever characteristic of this type of malignancy?

DR. BADGER Not unless there is some necrosis of tumor.

DR. YOUNG You might wonder why I operated on this patient. I did it purely on the basis of the possibility of metastatic cancer. I thought the gall bladder might be the primary focus.

REPORT ON MEDICAL PROGRESS

HEART DISEASE*

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BOSTON

THE challenging problems of heart disease provoke innumerable investigations. In the following brief report a few subjects have arbitrarily been chosen for discussion because of their clinical interest and practical bearing.

RHEUMATIC FEVER

Etiology

The intensive search for the causative agent of rheumatic fever based on the infectious theory of its origin has continued with interesting but as yet inconclusive results. Inoculation of material derived from human arthritic exudates, rheumatic pleural exudates or excised erythema nodosum nodules into the chorioallantoic membranes of chicken eggs has produced characteristic lesions.¹ Suspensions of these lesions when injected into mice caused pneumonia. Micro-organisms resembling the pleuropneumonia-like organisms isolated by Sabin² from normal mice were recovered from the lungs of such infected animals. Similar micro-organisms were more over cultured directly from human rheumatic exudates and produced the same type of pneumonia in mice. Suitable control studies failed to disclose such micro-organisms in non-rheumatic exudates. The pleuropneumonia-like micro-organisms studied by Sabin while morphologically similar to those isolated by Swift and Brown³ failed to induce pneumonia in mice. These findings are of considerable interest but further work will be required to demonstrate con-

clusively their etiologic significance in the causation of rheumatic fever.

The etiologic influence of various contributory factors is generally recognized. Rheumatic fever occurs most commonly in the temperate zones. It is relatively rare in the tropics and in the arctic regions and correspondingly, its onset in the temperate zone is relatively uncommon in the middle of the summer and during the cold winter months. The increased incidence of rheumatic fever in the lower economic groups emphasizes the etiologic importance of general hygiene, adequate nutrition and the effects of overcrowding. Rheumatic fever becomes prevalent during epidemics of upper respiratory infection and is prone to occur when scarlet fever is rampant. Following fully 50 per cent of the sore throats in rheumatic fever subjects,⁴ a recurrence of rheumatic fever occurs.

The factors of susceptibility and communicability of rheumatic fever have been stressed by several recent investigations. That heredity is of significance in addition to the factors of contagion and environment, is demonstrated by trustworthy recent evidence which is in accord with previous investigations.⁵⁻⁷ While the familial incidence has long been recognized it is not generally realized that it is in fact as high as that of tuberculosis.⁴ Rheumatic manifestations in the parents, aunts, uncles and grandparents of rheumatic patients are definitely increased over those in control groups.⁸⁻⁶ Between the patients and their siblings and parents there is usually contiguity as well as consanguinity but the uncles, aunts and grandparents of the patients, in the majority of cases, do not

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belong to the same household or to the same immediate environment. The finding of a familial tendency for at least three generations is strongly suggestive of a constitutional susceptibility to this disease. These findings do not, of course, contradict the etiologic significance of exposure and hygiene.

Clinical Characteristics and Diagnosis

Intelligent clinical care of the patient with rheumatic fever depends in large measure on the recognition of certain features emphasized by recent publications.

The chronicity of rheumatic fever. Characteristic symptoms and signs such as joint pain of varied degree, low-grade fever, subcutaneous rheumatic nodules, erythema marginata, frequent nontraumatic nosebleeds, abdominal or precordial pain, anemia,⁸ loss of weight or even failure to gain weight may persist for months or years. Sydenham's chorea has long been considered to be associated with rheumatic fever, and the relation is indeed close. Recent studies^{7, 9} have shown that, of those children exhibiting only chorea, approximately 50 per cent will within the following eight years show other manifestations of rheumatic fever. The incidence of heart disease in children with other rheumatic manifestations is approximately the same regardless of the presence or absence of chorea. The incidence of heart disease in those children who do not show other rheumatic manifestations, but who may have recurrence of chorea, is strikingly low, amounting to only 3 per cent. It therefore appears that chorea should continue to be regarded as frequently, although not invariably, signifying rheumatic infection.

Subclinical rheumatic fever. Evaluation of the presence or absence of active rheumatic fever is perhaps the most important feature to be determined in the clinical care of the patient with rheumatic heart disease or previous rheumatic fever. Medical attention has been directed too long to an appraisal of the degree of rheumatic heart disease or an interpretation of various cardiac murmurs. Clinical symptoms and laboratory tests indicative of the presence of active rheumatic fever have been minimized. It is important to recognize even subclinical rheumatic fever, since such patients are prone to exacerbations of the disease and must be protected from various events and placed at complete rest. It is the active disease, rheumatic fever, which is responsible for the fatal outcome in children and young adults.

With the cessation of the clinical manifestations of rheumatic fever, there is usually laboratory evidence of the continuation of the active process for

varying lengths of time, from two or three months to several years. This phase is denoted by an increase in the sedimentation rate of the red blood cells, repeatedly elevated leukocyte counts (above 10,000), and, less often, prolongation of auriculoventricular conduction time by electrocardiogram. The apparently silent development or increase in the development of rheumatic valvular involvement is readily understandable on the basis of these considerations.

Recurrences and recrudescences of rheumatic fever. It is unusual in childhood for the patient to have only a single attack. There is no evidence available which indicates definitely whether or not recurrences are an expression of reinfection. The severity of the individual recurrences is to a large extent the determining prognostic feature. Especially important with regard to recurrences are the first five or six years following the onset of rheumatic fever, since the disease most often recurs during this period. The majority of rheumatic fever subjects who do not develop considerable cardiac damage, especially cardiac hypertrophy, during this time have a good prognosis.

Certain events have been noted which seem to precipitate the clinical manifestations of rheumatic fever. Exacerbations are often associated with upper respiratory infections. Usually, rheumatic fever develops within one to three weeks after such an event, there being at times a so-called silent or latent period. The frequency of recurrences of rheumatic fever following such a procedure as tonsillectomy is too often disregarded. Other operative procedures, accidents such as broken bones, severe sunburn, extraction of teeth and a variety of minor non-streptococcal illnesses have been observed to precipitate rheumatic fever. Injection of stock typhoid vaccine (0.1 cc of vaccine containing 250,000,000 organisms), resulting in a moderate temperature reaction and a child likewise may reactivate quiescent rheumatic infection.¹⁰

As with other conditions which have attracted widespread interest and study, the positive diagnosis of rheumatic fever is not infrequently made falsely, the patient is crippled not by the disease but by the diagnosis. Recent studies¹¹⁻¹³ on the significance of so-called growing pains in children exonerate these vague muscular pains and ache in the lower extremities from the ominous significance attributed to them by some clinicians.

In a number of recent publications, patients with so-called growing pains have been considered as rheumatic subjects. Shapiro^{11, 13} states, however, that growing pains are not due to rheumatic infection, and that the great majority of children who complain only of leg pains are not suffering

from rheumatic fever. In a follow up study of 200 children who complained only of leg pains Shapiro found that none developed rheumatic heart disease. The salient diagnostic characteristics of

TABLE 1 Differences Between Nonrheumatic Growing Pains and Joint Pains of Subacute Rheumatic Fever 13

	NONRHEUMATIC GROWING PAINS	JOINT PAINS OF THE SUBACUTE RHEUMATIC FEVER
Age at onset	Early childhood; often continues through adolescence.	Most commonly between 6 and 7 years of age; often occurs in attacks following prior respiratory infections or other infectious diseases.
Time of pain	At end of day especially during night, often awakening the child several times; pain is gone in the morning and usually does not occur during the day.	On first getting out of bed in the morning and during entire day especially on motion; of ten causing limp; patient feels better on getting warm in bed.
Location of pain	Most commonly in muscles of legs and thighs rarely in muscles of upper extremities; occasionally in elbows and knees.	In joints—usually in upper and lower extremities.
Other signs of rheumatic activity	Usually none.	Repeated bouts of joint pain, sometimes accompanied by fever and rash.
Objective signs in joints	None.	Joints often have slight increased local heat and mild swelling usually overlooked by patient and parent.
Family history of rheumatic fever	Uncommon.	Common.
Laboratory findings	Normal sedimentation rate; normal leukocyte count; normal hemoglobin.	Increased sedimentation rate; mild increase in leukocyte count; moderately decreased hemoglobin.

be borne in mind in the differential diagnosis of growing pains and of joint pains of subacute rheumatic fever are shown in Table 1.

Prognosis The paucity of reliable statistics regarding so widespread a disease is remarkable. Jones⁴ has summarized his observations on 1000 subjects with rheumatic fever followed for an average period of ten years from the onset.¹⁴ The average age of onset was eight, the average age at the time of the last observation was eighteen, hence the data represent the first decade of rheumatic fever. Of this group 242 were dead, 310 had no demonstrable rheumatic heart disease, 427 patients had definite rheumatic heart disease and in 21 the data were insufficient. It is somewhat encouraging to know that in this large group of patients nearly 60 per cent were able to carry on a normal physical life ten years after the onset of their disease. In an encouraging percentage, clinical evidence of rheumatic heart disease regresses or even disappears.

Treatment

Sulfanilamide The effectiveness of sulfanilamide and its derivatives in a wide variety of in-

fectious states led to the hope that the active manifestations of rheumatic fever might likewise prove responsive to these therapeutic agents. The close relation of rheumatic fever to hemolytic streptococcus respiratory infections lent encouragement. Convincing studies have demonstrated, however, that sulfanilamide exerts no beneficial effect on chorea or on active rheumatic infection in any of its stages.^{15, 16} On the contrary, an increased incidence of toxic reactions to sulfanilamide has been observed in patients with manifestations of active rheumatic infection. There is no evidence that sulfanilamide produces any symptomatic relief or abridgment of the illness.

In patients with rheumatic heart disease suffering from acute hemolytic streptococcus respiratory infection the question not infrequently arises as to the advisability of sulfanilamide therapy. Conservative clinical judgment must be exercised in such cases, particularly since the incidence of recurrence of active rheumatic fever following sulfanilamide therapy is not decreased and may be increased. Encouraging results^{17, 18} have been reported regarding the prophylactic value of sulfanilamide in quiescent cases in preventing streptococcal throat infections and associated exacerbations of rheumatic infection. The general use of sulfanilamide for this purpose cannot be advised until considerably more evidence has accumulated. In general it must be concluded that sulfanilamide is valueless and even dangerous in the treatment of active rheumatic fever.

Tonsillectomy and foci of infection Since the etiology of rheumatic fever is closely associated with streptococcal infection, the removal of foci of infection especially tonsils and adenoids, has been a major feature of the treatment of the disease. There is at present no distinct agreement concerning the value of such a procedure, particularly since so many patients have had a tonsillectomy performed prior to the onset of rheumatic fever.¹⁹ It has previously been suggested that tonsillectomy be performed during the height of rheumatic fever, but this practice has been discarded. It would seem wise in general to advise tonsillectomy in a patient with a history of very frequent sore throats, but only in the absence of clinical and laboratory evidence of active rheumatic fever. In this way many recurrences of rheumatic fever will be avoided. Extraction of teeth should also, if possible, be carried out in the absence of active rheumatic fever for fatal recurrent rheumatic fever may follow such a procedure.²⁰

Other measures In the absence of any proved specific measures for treatment of rheumatic

fever, reliance must be placed on the use of salicylates whenever necessary for the comfort of the patient, absolute bed rest, the judicious use of sedatives, a diet containing all essential elements and the establishment of a satisfactory psychologic adjustment to the illness.

CALCAREOUS AORTIC STENOSIS

This cardiac lesion, frequently overlooked and predisposing to sudden death, has continued to stimulate considerable interest.

Aortic stenosis in young individuals with obvious rheumatic heart disease is comparatively common and offers little difficulty in diagnosis. Calcareous aortic stenosis, on the other hand, is prone to occur or be discovered relatively late in life predominantly in men who have no antecedent rheumatic history. The symptoms of cardiac asthma, congestive heart failure or angina pectoris as a rule cause the patient to seek medical advice. He usually shows considerable cardiac enlargement, together with a slow pulse rate and normal or decreased pulse pressure. The absence of any obvious etiologic cause for the cardiac symptoms other than general arteriosclerosis, together with the slow pulse and cardiac enlargement, should lead one to suspect calcareous aortic stenosis as the cause. The diagnosis is confirmed by the presence of a thrill and systolic murmur in the aortic area, transmitted upward into the carotid artery and often accompanied by a diastolic murmur.

The lesion and its symptoms are likely to appear late in life and progress slowly. It is important to realize, however, that the prognosis is poor. The symptoms respond poorly to therapy and sudden death is common.²⁰⁻²² This is of particular importance when considering the advisability of surgical procedures.

The lack of adequate information concerning the etiology has been the cause of considerable interest and speculation. The lesion was first described accurately by Monckeberg in 1904, and has been ascribed as resulting from atherosclerosis, from some unidentified form of chronic inflammation, from some toxin and from rheumatic fever, and the idea has been advanced that the lesion represents the healed vegetations of subacute bacterial endocarditis.

Christian²³ in 1931 subscribed to the rheumatic etiology of calcareous stenosis of the aortic valve, a view supported by others.²⁴⁻²⁵ Recent studies²⁶ indicate that in the cases with mitral valvular deformity, rheumatic etiology is predominantly responsible while in the cases of pure aortic valvular stenosis without mitral involvement arteriosclerotic degeneration is often responsible. The

fact that this type of aortic valvular disease is a clinical entity does not necessarily indicate that it is an etiologic entity. Arteriosclerotic degeneration and rheumatic fever are each probably responsible in different cases.

MEDICINAL TREATMENT OF ANGINA PECTORIS AND MYOCARDIAL INFARCTION

The object of medicinal treatment is to control the symptoms and functional disorders of the heart and circulation. There are no chemical agents that are known to influence materially the course of the structural abnormality in the myocardium or coronary arteries. The treatment of angina pectoris must be varied and adapted to fit the individual needs of each patient. In some cases an abnormality of the blood or basal metabolism or an unusual sensitivity to coffee or tobacco may be an important factor. In others, careful study of the patient's daily routine and contacts with people may reveal a constant relation between the occurrence of attacks and emotional factors or habits of eating which may be avoided or corrected. Surgery may be advisable in a few. In most patients, however, the skillful use of drugs, singly or in combination, is of paramount importance in the treatment of angina pectoris.

The problem of drug therapy in angina has been the subject of many studies. Evans and Hoyle²⁰ and more recently Gold and his associates²⁷⁻²⁸ have thrown doubt on the efficacy of medicinal therapy in angina, for they found that clinical improvement followed placebo medication as often as it did the use of drugs of reputed value. Riseman and his co-workers,²⁹⁻³⁰ instead of relying solely on clinical impressions, have also measured the amount of work under standard conditions which patients could perform before heart pain developed. According to these carefully controlled objective measurements, certain drugs were found to be of distinct therapeutic value. A knowledge of certain characteristics of these drugs is of considerable practical importance in their clinical use. More recently Levy and his associates³¹ have shown that certain of these drugs prevent or delay the production of the electrocardiographic changes induced by anoxemia in patients with angina.

The Nitrites

Nitrites are generally acknowledged to be of great value in the pain of angina pectoris, but certain useful aspects have been stressed in recent communications. While many patients experience marked benefit from nitroglycerin, others derive no beneficial effects and in a few the

attacks are aggravated²² Certain patients are unusually sensitive to the disagreeable effects flush, headache, throbbing and sensation of tension in the head, palpitation and even giddiness and fainting Rarely patients may show marked pallor, perspiration and a fall in blood pressure but no electrocardiographic changes following the administration of 1/100 gr of nitroglycerin For all practical purposes 1/200-gr hypodermic tablets are usually as effective as 1/100-gr ones and are rarely associated with any untoward effects 1/500 gr is less effective.²³ In all cases, much is to be gained by administering a test dose in the office or at the bedside and personally observing the effects.

The use of tablets which dissolve readily under the tongue, such as those prepared for subcutaneous use, are to be preferred The ordinary tablet triturates frequently have little or no effect on the duration of pain Hypodermic tablets dissolve completely in fifteen or twenty seconds and only rarely require as long as twenty seconds The tablet triturate and the granules require one or two minutes for complete solution

While the commonest use of nitroglycerin is to decrease the duration of pain, the drug has a prophylactic value which has received insufficient attention^{24 25} Murrell's original communication²⁴ advocated the administration of nitroglycerin several times a day in order to prevent attacks, and more recently its use immediately before exertion is undertaken has been suggested²⁵ Rise man and Brown²⁶ observed that approximately one third of their patients could be rendered completely free of attacks by taking 1/500-gr hypodermic tablets under the tongue at hourly intervals during the day For preventing attacks it is important to realize that small doses (1/500 gr) are quite as effective as large doses

Patients often inquire whether the frequent use of nitrites will eventually lead to dependence on the drug, and whether such use reduces the efficacy of the medication The patient may be assured that neither of these consequences will occur

All the nitrites act qualitatively alike The perle of amyl nitrite, commonly used by inhalation, is usually not so satisfactory as the tablet of glyceryl trinitrate The cost and the odor which may be especially marked if released in a closed room are definite drawbacks to its use Furthermore, absorption from the lungs is more rapid than that from the sublingual tissues, and since the exact dose cannot be determined accurately alarming symptoms may be precipitated in patients who inhale deeply An interesting contribution to the subject of nitrite therapy was

recently published by Krantz and his collaborators²⁷ They prepared octyl nitrite, a liquid less volatile and less potent than amyl nitrite Octyl nitrite inhalers are still in the experimental stage, and clinical evaluation is necessary before its usefulness in the treatment of angina pectoris can be determined Levy²⁸ recommends erythrol tetranitrate in a dose of 1/2 gr (0.03 gm) at bed time to control attacks of pain which are likely to occur during the night Sodium nitrite, long in favor, is used less commonly, primarily because more potent preparations are available This drug is not stable, and on standing forms the less effective nitrate

There is some hazard in the use of nitrites in the acute phase of myocardial infarction The nitrites by causing a fall of blood pressure reflexly stimulate the cardiac accelerators and may precipitate dangerous ectopic tachycardias By further lowering the blood pressure, which may already have fallen considerably the blood flow in the patent coronary vessels and hence the collateral circulation may be impaired since the efficiency of the coronary circulation depends in great measure on an adequate level of systemic pressure.

Xanthines

Since attention was first directed to the use of the purine bases in the treatment of angina pectoris,²⁷ numerous preparations have been advocated Theobromine and theophylline are not soluble in water, but when mixed with ethylene diamine, or certain salts such as sodium acetate, they readily go into solution Many preparations using various soluble salts and with dubious claims have been offered to the profession at exorbitant prices which impose a considerable financial burden on the patient Of the theobromine preparations, theobromine sodium acetate in doses of 71/2 gr (0.5 gm) given four times a day appears to be far superior to all other preparations of theobromine and is as effective as the best of the theophylline compounds²⁹ From the practical standpoint, it is pertinent that the cost of a week's supply of theobromine sodium acetate on prescription is approximately 45 cents, compared to a cost of \$1.50 for most other preparations on the market Theophylline sodium acetate is as effective as theobromine sodium acetate This preparation has the advantage of being effective in a smaller dose than the theobromine salt and therefore a smaller size tablet is available For years this has been a proprietary preparation but it is now being made available by several drug houses

There has been considerable comment in the literature concerning the possible cerebral effects

of the purines. This is probably suggested by their chemical relation to caffeine. No evidence of cerebral stimulation or kidney irritation has been presented.

The incidence of gastric distress can be reduced by coating the tablets so as to prevent contact with the gastric mucosa. The use of enteric coatings has outstanding value, but it must be remembered that an effective enteric coating delays absorption for four or five hours. Under such conditions a final dose just before retiring is of great importance, for otherwise the patient is without medication until the morning dose becomes available sometime in the early afternoon. In some cases it is advisable to give an uncoated tablet in the morning in addition to the enteric-coated tablets.³⁸ It must also be remembered that the use of strong cathartics may hurry the enteric-coated pill through the intestinal tract undissolved and hence prevent absorption.

In general, the frequency and degree of improvement increase as the dose is increased. All theobromine and theophylline derivatives cause nausea and heartburn when given in sufficiently large amounts, and when this gastric distress becomes severe, any improvement induced by small doses disappears. The optimum dose for most patients is the maximum amount that can be given without causing severe gastric distress, in a few cases equally satisfactory improvement can be obtained with somewhat smaller doses. Whether a patient with angina will respond to the purines and what the optimum dosage will be cannot be foretold, each patient must be individually studied.

In the treatment of cardiac infarction, the intravenous administration of theophylline ethylenediamine (Aminophyllin, Metaphyllin, Euphyllin, Carena, Inophylline) may be effective in alleviating pain. A dosage of 4 gr given slowly has been recommended³⁹ but somewhat larger doses may be employed.

Tissue Extracts

Rumors as to the clinical effectiveness of tissue extracts have been frequent since their introduction by Schwarzmann in 1929.⁴⁰ No objective evidence exists that they are of value.

Quinidine

The use of quinidine sulfate in angina pectoris was recommended by Proger, Minnich and Magendantz.⁴¹ The exact mechanism whereby its effect is achieved is unknown. Riseman and Brown³⁰ believe that this drug should be used more frequently in the treatment of angina. Doses of 5 gr (0.3 gm) four times daily give striking benefit in many cases. An occasional patient may prove to be hypersensitive or show an idiosyncrasy

to this drug, but such individuals are rare, diarrhea of moderate severity is commoner, in such cases the dose should be decreased.

Quinidine is also useful in the treatment of auricular flutter and paroxysmal auricular or ventricular tachycardia which may be accompanied by angina pectoris, and prophylactically in cases of myocardial infarction which show numerous ventricular extrasystoles.

Sedatives

The use of sedatives such as the barbiturates in small, repeated doses is of considerable value in patients with angina pectoris. They probably lessen the sensitivity of the patient to emotional stimuli, and may also decrease the rate at which exercise is undertaken in daily life. Only moderate doses are advocated such as $\frac{1}{4}$ to $\frac{1}{2}$ gr of phenobarbital three times a day. It is inadvisable, however, routinely to combine the sedative with other drugs in a single tablet or capsule in fixed proportions, for the optimum dosage of each ingredient varies for different patients.

Morphine

While fully agreeing with the widespread use of morphine in cases of myocardial infarction, Gold²⁷ cautions that it sometimes complicates the course of myocardial infarction. It promotes constipation with abdominal distention, and urinary retention through spasm of the bladder sphincter. It also causes vomiting, which may be repeated over a period of several hours. This violent muscular effort is a source of danger in myocardial infarction. It is also a source of confusion in that one may be at a loss to determine whether the vomiting is due to the drug or to the myocardial infarction itself. Morphine causes strong vagal stimulation, and this renders the heart more susceptible to auricular and ventricular ectopic rhythms. Gold states, "One may well ask how often ventricular tachycardia after coronary thrombosis is due in part at least to the morphine with which the condition was treated."

The following plan is applicable in the majority of cases: $\frac{1}{4}$ gr (0.016 gm) of morphine sulfate by subcutaneous injection, repeated at intervals of one-half hour until the pain is abolished or reduced to a minimum. The interval between doses should not be shorter, and to give more than a total of 1 gr (0.065 gm) in twelve hours is rarely wise. Larger doses than 1 gr are rarely more effective in quieting the pain.

Severe pain, its attending anxiety and the distress of paroxysmal dyspnea are the three major indications for the use of morphine in the course of myocardial infarction. The vague notion is

entertained that morphine exerts a direct beneficial effect in coronary thrombosis independent of its influence on symptoms. There is no sound justification for this view.

Codeine in $\frac{1}{2}$ or 1 gr doses may occasionally be used with advantage as a substitute for morphine in mild cases, or in order to obviate the danger of withdrawal of symptoms in prolonged cases. Although dilaudid and pantopon are widely used, it is doubtful whether they have any advantages over morphine in this condition. If the patient is intolerant to morphine, so that ordinary doses cause vomiting or excitement, a combination in a capsule of $\frac{1}{2}$ or 1 gr of codeine with 1/150 gr of scopolamine hydrobromide or with 1 gr of phenobarbital will occasionally provide a satisfactory substitute.²¹

In cases in which pain is resistant to other measures, placing the patient in a tent with oxygen of about 50 per cent concentration is sometimes useful. It is especially indicated in patients with cyanosis or respiratory distress. While codeine and the other opium derivatives are clearly of value in the treatment of cardiac pain they are of course unsuited for prolonged use.

Digitalis

The use of digitalis in angina pectoris and myocardial infarction continues to be widely debated. It is generally agreed that three conditions indicate the administration of digitalis: congestive heart failure, paroxysmal dyspnea and certain abnormal rhythms such as auricular fibrillation with rapid ventricular rates, auricular flutter and occasionally paroxysmal auricular tachycardia. A patient with these disorders should receive digitalis regardless of what accompanying conditions are present. The effect of digitalis in congestive failure and certain paroxysmal arrhythmias is to enable the heart to accomplish increased output and increased external work.

Most patients with myocardial infarction do not fall into any of the above categories and do not require digitalis. The manifestations of shock in patients with myocardial infarction are due to peripheral vascular collapse; digitalis is not more efficacious in this situation than it is in the peripheral vascular failure of pneumonia, sepsis or traumatic shock.

Patients with coronary arteriosclerosis not infrequently show partial heart block with either a prolonged PR interval or a 3:2 or 2:1 auriculo-ventricular response. The question then arises whether, in the presence of positive indication for the use of digitalis, the drug should be withheld lest it increase the heart block and possibly produce complete auriculoventricular dissociation, with its hazard of ventricular standstill. Contra-

dictory statements by acknowledged authorities and the absence of any body of evidence suggested the desirability of a study of this question by Altschule and myself.⁴ The results of this study demonstrated that partial heart block is unaffected by digitalis in moderate therapeutic doses and that this drug should not be withheld in the face of positive indications.

A satisfactory dose in the average case of auricular fibrillation or heart failure in myocardial infarction is about 0.4 gm of digitalis leaf daily for two days, followed by about 0.1 to 0.3 gm a day as long as necessary. The patient should be watched carefully for the appearance of increase in the number of ventricular premature beats, which should serve as a guide to reduction of the dose.²²

In patients with angina pectoris, digitalis is the subject of a wide divergence of opinion. Gold and his associates⁴² reported that not one of their 120 cases of angina pectoris of effort was influenced unfavorably by even toxic doses of digitalis, and concluded that no direct constrictor action was exerted on the coronary circulation in patients with coronary artery disease. They believe that while patients within three weeks after myocardial infarction may react unfavorably to complete digitalization, doses of approximately three-fourths of those which would be given if the patients did not have a myocardial infarct involve no special hazard.

In patients with angina of effort in whom evidence of congestive failure is found, administration of digitalis should improve the general circulation, including that of the heart. In uncomplicated angina, Riseman and Brown²³ observed that digitalis was rarely of value and frequently caused a striking increase in anginal attacks. This is in accord with the observations of Fenn and Gilbert.⁴⁴

Potassium Iodide

While potassium iodide is of undoubted value in the treatment of the cardiac pain associated with syphilitic heart disease or thyrotoxicosis, no evidence of its value in other conditions is available.

No adequate means exist at the present time of predicting which drug will benefit a given patient with angina pectoris, or indeed whether the patient will respond to any medication in any degree. It is to be remembered that drug therapy is only one factor in the medical management. The regulation of the patient's dietary regime and program of activities, the wise adjustment of emotional factors, the use of moderate doses of alcohol and the correction of anemia, thyrotoxicosis or other organic ailments are of importance.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25421

PRESENTATION OF CASE

A sixty-seven year-old retired business man was admitted complaining of severe substernal pain of thirty seven hours duration.

At 2:30 a.m. while in bed, thirty seven hours before admission, the patient was suddenly awakened by a severe substernal and midepigastrie, "raw and oppressive, non radiating pain, which "practically took his breath away and which was unassociated with cough, sputum, hemoptysis, palpitation or evident cyanosis. He had difficulty in getting his breath because of a sharp stabbing pain on deep inspiration. He arose, felt weak but walked across the room and applied rubbing alcohol to the anterior chest. When he returned to bed he was forced to remain in the sitting position because of orthopnea. The persistent pain prevented his return to sleep. Throughout the day before entry he was nauseated and noted malaise and anorexia. He was able to climb one flight of stairs without unusual dyspnea and failed to notice any increase in the still persisting substernal discomfort. The evening before admission he was awakened every ten to fifteen minutes by the pain which forced him to sit upright in bed. On arising at 10 a.m. on the day of admission the pain and nausea were much more severe. He had retching but did not vomit. He was seen by a physician at noon and referred immediately to the hospital.

Two months before entry the patient had developed a painless tumor in his nose which grew steadily and caused complete obstruction of the nasal passages, with an associated epiphora. A biopsy of the tumor taken in the Out Patient Department two days before admission showed it to be a "lymphoblastoma reticulum-cell sarcoma type." On the same day x-ray studies had been made. The family, marital and past histories were noncontributory.

The physical examination revealed a lean, suntanned man sitting up in bed and complaining of pain in the lower midanterior chest on deep inspiration. There was epiphora of the right eye. The fundal vessels were slightly arteriosclerotic. The nose was completely obstructed by a painless, irregular, red growth which bled easily and

which seemed to arise from the septum. The few remaining teeth were dirty and carious. The chest was rather flat and somewhat splinted on both sides. The heart was apparently not enlarged. The apex was in the fifth interspace in the mid clavicular line, 10 cm. to the left of the sternum. The apical sounds were of good quality, but there was a suggestion of tic-tac quality over the remainder of the precordium. The aortic second sound was louder than the pulmonic. On admission to the ward at 3 p.m. there was present a definite to-and-fro apical friction sound, but four hours later it could not be heard. The pain on deep inspiration had also almost completely disappeared. The remainder of the examination was essentially negative.

The temperature was 98°F., the pulse 70, and the respirations 19.

The blood examination was normal. The urine sediment showed 10 to 15 white blood cells per high power field. An electrocardiogram taken on the first hospital day showed a normal rhythm of 110 with a PR interval of 0.14 second, ST₁ and ST₂ were slightly elevated, T₂ was inverted, the QRS complexes in Leads 1, 2 and 3 were low, there was slight left axis deviation.

In the early morning of the first hospital day the patient was awakened by a persistent recurrence of the original chest pain, and a friction rub, pericardial in timing, was heard over the apex in the fifth left interspace. There was tachycardia. Fifteen hours later the friction sound was gone. During this interval the electrocardiogram mentioned above was taken. On the third hospital day the patient was comfortable and had no pain, and the heart was normal on physical examination. An electrocardiogram showed a normal ventricular rate of 80, the PR interval was 0.13 second, with late inversion of T and T₂, ST₂ and ST₃ were slightly elevated, there was low voltage of the QRS complexes in Leads 1, 2 and 3, and a slight tendency to left axis deviation. On the fifth hospital day the temperature rose to 100.2°F., but the pulse and respirations remained at 86 and 20 respectively. On the tenth hospital day the corrected sedimentation rate was 1.8 mm. per minute, and the white-cell count 10,300. The patient was in no discomfort. The skin was dry, and there was no cyanosis or signs of heart failure.

He seemed well enough so that on the seven tenth hospital day x-ray treatment of the nasal lesion was begun. He was given a 400-r daily dose to a total of 1200 r per nasal field. At the same time an electrocardiogram showed a ventricular rate of 100, normal rhythm, low T₁ and inverted T₂, T₃ and T₄, with slight improvement in the voltage as compared with the previous rec-

ord After completion of x-ray therapy on the twenty-second hospital day the nasal lesion appeared smaller, and there was a beginning air passage through it. There was a slight temperature rise to 101°F, with a pulse of 110 and respirations of 30, as the only apparent evidence of x-ray reaction. Later, however, he developed severe frontal and nasal head pain requiring morphine for relief. On the thirty-first hospital day at 4:15 p.m. he developed an acute, severe, right shoulder pain, associated with a drop in blood pressure to 82 systolic, 70 diastolic, and the presence of cold clammy hands. The heart rate was 110, with irregular rhythm, weak sounds and an intermittent gallop. He became cyanotic, and one hour later he developed Cheyne-Stokes respirations and his blood pressure was not obtainable. He quickly failed and died.

DIFFERENTIAL DIAGNOSIS

DR EDWARD F. BLAND We are presented here with the record of a patient in whom the diagnosis of malignant lymphoma had been established. Although we know that this is an ultimately fatal disease, I think we have reason to suspect that this patient died rather prematurely. We might have expected that he would have lived several months longer and probably several years with adequate treatment. My x-ray colleagues assure me that a 1200-r exposure to the local lesion in three days is fairly vigorous treatment for each nasal field. Dr. Edward Gall has pointed out that this type of lymphoma is not quite so radiosensitive as are some of the others. We have clear evidence, however, that the nasal lesion was responding favorably to x-ray therapy.

Our problem is to determine why this patient died prematurely with a series of rather alarming episodes, the first of which precipitated his admission to the hospital and the fourth of which was responsible for the fatal termination. The episodes which occurred in the hospital followed a general pattern. They varied somewhat in detail. The first characteristic which warrants some attention is that they were all abrupt in onset. It was interesting that the first occurred during the night following the patient's visit to the Out Patient Department when he had had a biopsy taken and had x-ray studies and probably some unusual manipulation of his neck. The type of pain, it seems to me, was somewhat more characteristic of pleural origin than it was of cardiac origin, it almost certainly was not associated with coronary insufficiency, but it might have been of pericardial origin. Pericarditis may be an uncomfortable condition although often

it is unaccompanied by actual pain. I think it is rarely associated with very severe pain such as this patient apparently had.

His heart and circulation seemed to have been in relatively good condition and without abnormal physical signs throughout the course of the fatal illness, until the last episode, except that I am a little in doubt as to the exact nature of the friction sound which was described as being fairly localized in the vicinity of the cardiac apex and pericardial in timing. I am inclined to think that this was of pleural or perhaps pleuropericardial origin rather than due to uncomplicated pericarditis. Pericardial friction rubs are ordinarily best heard over the body of the heart, either to the right or left of the sternum. It would be a little unusual then to have the sound localized so far out. Furthermore, the absence of tachycardia or any other indication of serious involvement of the heart itself seems to me somewhat against a purely pericardial origin.

Then we come to the electrocardiogram. It is quite evident that the heart was under grave suspicion. They took three electrocardiograms. The findings are abnormal but somewhat inconclusive as to the exact nature of the trouble. This patient was in the age group in which one expects some sclerotic changes in the coronary vessels. These abnormal electrocardiographic changes could have been due to underlying coronary disease or possibly secondary to acute cor pulmonale. Furthermore, they might have been the result of pericardial involvement.

Throughout the record nothing is said about x-ray studies of the chest. Dr. J. H. Means* has recently called our attention again to the extraordinary capacity of lymphoma for simulating other clinical conditions. We should like very much to know by x-ray study if there was any suggestion of cardiac or pericardial abnormality or any indication of involvement by the lymphomatous process of the thoracic viscera. No therapy was directed toward the chest, so I think we must assume that chest films were not taken and that no suspicion of a thoracic lymphomatous lesion was entertained by those in charge of the patient. At least I cannot otherwise explain why no mention is made of a chest film. However, I think we must accept its absence, but with some reservation, as evidence against lymphomatous involvement of the thoracic viscera. But so far as I am concerned, it is not only conceivable, but we know, that lymphoma may rather silently infiltrate the pericardium and give rise to pericarditis and a large pericardial effusion. Lym-

*Means J. H.: The symptomatology of lymphoma. J. A. M. A. 113:646-649, 1939.

phoma may also invade the myocardium itself.

DR. TRACY B. MALLORY The chest was never x-rayed, so far as I can make out from the record.

DR. BLAND Then we come to the final episode which, I think, is of considerable interest. It was preceded by a headache severe enough to require morphine. X ray therapy directed toward the head, I am told, may cause some increase temporarily in intracranial pressure, but I think that a headache of this order is most unusual as a result of local x ray therapy. Of course there was an extensive lesion in the nasopharynx, and possibly secondary infection. On the other hand, in view of the subsequent events, we wonder if this headache may have had another basis. Shortly thereafter, — we do not know exactly how soon — this patient abruptly went into collapse, with severe pain in the right shoulder, which suggests to me either a pleural origin from the right upper portion of the lung or referred pain from the diaphragmatic pleura.

There are two possible explanations for this final fatal episode which appeal to me. On the basis of the data given in the record, lymphomatous infiltration of the pericardium and heart seems least likely of the two possibilities, both because of the abruptness of the acute episodes with associated severe pain and because of the nature of the final attack. I suppose it is possible that a pericardial effusion may have been developing and escaped detection. It is sometimes very difficult to detect even a large pericardial effusion, especially if it is located posteriorly and not suspected. It would be somewhat difficult on the basis of a diagnosis of final cardiac tamponade secondary to pericardial effusion to explain the abrupt severe pain in the right shoulder. Cardiac tamponade from pericardial effusion is usually not a very painful event. It is possible, I suppose, that this patient may have had some associated coronary insufficiency, but it seems to me again very unlikely that the terminal event was related to failure of the coronary circulation. It does seem to me possible and perhaps the more likely of the two possibilities that this final illness and the patient's premature death were secondary to recurring pulmonary emboli with pulmonary infarction. One would like to speculate a bit as to the possible source, if this should prove later to be the correct impression. I was impressed by the apparent severity of the headache a day or two before the terminal illness and by the initial episode following a certain amount of manipulation of the head and cervical region, and I am wondering if a deep cervical phlebitis or a phlebitis of the veins at the base of the skull might not have been the source. In

conclusion I suggest, as my first choice of the above two possibilities, that this patient had lymphoma of the nasopharynx and recurrent pulmonary emboli with infarction and possibly terminal acute cor pulmonale.

DR. PAUL D. WHITE I have nothing to say except that we see very rare cases of tumor that involve the heart and pericardium with signs and symptoms that are indistinguishable from other types of heart disease, for example coronary disease.

CLINICAL DIAGNOSES

Reticulum-cell sarcoma of nose.
Coronary occlusion

DR. BLAND'S DIAGNOSES

Lymphoma of nasopharynx
Pulmonary emboli and infarction
Acute cor pulmonale?

ANATOMICAL DIAGNOSES

Reticulum-cell sarcoma of nasopharynx, mediastinum, pericardium, myocardium, adrenal glands and kidneys.
Hemopericardium
Pulmonary congestion and edema
Operative scar suprapubic prostatectomy

PATHOLOGICAL DISCUSSION

DR. MALLORY On the wards it was assumed that there was a cardiac complication in this case and in all probability that it was coronary occlusion. The determination of the exact mechanism of death is often extremely difficult either clinically or anatomically, and there remain a very large number of cases in which we totally fail to do so.

We found that the lymphomatous process was much more extensive than had been suspected clinically. Not only did it involve the ethmoid sinuses and nares but there was extensive mediastinal disease, involvement of the adrenal glands and kidneys, and a massive involvement of the pericardium and of the heart itself. There was a fibrous pericarditis but no pleuritis, so I think that the friction sound was a true pericardial rub. The major portion of the left ventricle and a large portion of the right showed massive tumor infiltration and the coronary arteries appeared to be considerably narrowed by external pressure of tumor in the epicardium, but were nowhere occluded and there were no thrombi. The brain was negative and I have no anatomical grounds on which to explain the headache. I should simply raise the point that it is not in

frequent to see considerable edematous swelling of a tumor immediately following x-ray treatment, and I think swelling of tumor in the region of the ethmoid sinuses might have accounted for the sudden accession of pain. The sudden and marked swelling of a tumor following radiation is of most practical importance in relation to the treatment of lymphoma of the mediastinum. On several occasions where radiation has been given without first putting down a tracheal tube, we have seen sudden death from asphyxiation.

DR BERNARD M. JACOBSON: Was there anything in the appearance of the heart to suggest that a clue to the true diagnosis might have been supplied if we had had an x-ray film of the chest?

DR MALLORY: I do not believe it would have made much difference. The mediastinal involvement was great enough to have been observed and one might have guessed an extension from the mediastinum into the pericardium, but I do not believe one could have differentiated pericardial involvement and cardiac involvement.

DR JACOBSON: On account of the rather strong likelihood of fresh coronary thrombosis, it was a week or ten days after admission before we thought it was wise to move him to the x-ray treatment room. We still did not feel justified in putting him through a strenuous diagnostic routine.

DR MALLORY: The most puzzling feature of the case is, Why, with a slowly progressive infiltration of the heart, did the symptoms come on with such dramatic suddenness? I have no explanation for that.

DR BLAND: I suppose then there was terminal acute cardiac tamponade?

DR MALLORY: That would be hard to guess about rationally. The amount of fluid in the pericardium was not very large. On the other hand the pericardial wall was unusually thick and stiff.

DR WHITE: Was it thick all around?

DR MALLORY: Yes.

CASE 25422

PRESENTATION OF CASE

A fifty-four-year-old married machinist was admitted to the hospital complaining of severe frontal and occipital headaches of a year's duration.

One year before admission, without apparent precipitating cause, the patient first experienced the onset of attacks of dull, boring, frontal headaches, which characteristically moved backward over the course of twenty-four to forty-eight hours to the region of the occiput where they remained

for a few hours and then passed away. These headaches were accompanied by some dizziness and impairment of vision and occurred about twice a week. He changed his spectacles, but his symptoms continued. Five weeks after the onset of the headache, the patient consulted his family physician who found a systolic blood pressure of 220 and immediately advised bed rest, with the elimination of salt, spices and meat from his diet. Following this regime for about a month, the blood pressure was somewhat lower and he returned to work. His nocturia meanwhile increased to two to three times per night. He remained at work until two months before admission, although he was troubled by increasingly severe and frequent headaches with dizziness and scotomas. The diet consisted mainly of milk, cereal, bread, fruit and a little water. A few months before entry his blood pressure was 194 systolic and his local physician again advised bed rest. Two to three weeks before entry he became increasingly nervous and nauseated and on one occasion had a spontaneous nosebleed. The patient noted that his headaches were induced and aggravated by fear of losing his job and by other financial and family worries. On the evening before entry while lying in bed he became very dyspneic. His appetite had been only fair during this period of illness, and he had lost about 40 pounds in weight. On occasions he vomited greenish liquid material without blood.

For ten to fifteen years before admission the patient had noted nocturia, he was awakened from sleep once every night and passed a large quantity of urine. Three years before entry he changed his spectacles because of a recession of near vision. He had been constipated for the year prior to entry and had noted numbness and tingling of the fingers for six months. There had been no cough, orthopnea or ankle edema. There was no history of frequent sore throats or scarlet fever.

The family, marital and past histories were otherwise unremarkable.

Physical examination revealed a fairly well developed and nourished pale man lying flat in bed with little discomfort. He weighed about 135 pounds. The eyes showed bilateral swelling of the disks, with flame-shaped hemorrhages and recent and old exudates in the fundi. A few teeth were carious. The heart was enlarged to the left, 4 cm beyond the midclavicular line. The sounds were of good quality, with no thrills or murmurs. The rhythm was regular. The blood pressure was 236 systolic, 140 diastolic. There were a few fine crackling rales at the right base. The abdomen was normal.

The temperature was 99.6°F., the pulse 92, and the respirations 20

Examination of the blood showed a red-cell count of 3,000,000 with 45 per cent hemoglobin, and a white-cell count of 11,000 with 84 per cent polymorphonuclears. The smear showed moderate anisocytosis. The urine was clear with a pH of 6.5, a specific gravity of 1.010, a +++ albumin, no sugar, diacetic acid or bile, and 3 to 5 red cells, 3 to 5 white cells and many granular and hyaline casts per high power field. The serum calcium was 9.69 mg per 100 cc., the phosphorus 3.64 mg., the phosphatase 6.28 units, and the nonprotein nitrogen 75 mg. A blood Hinton test was negative. A phenolsulfonphthalein excretion test showed 2 per cent in fifteen minutes and a total of 7 per cent in an hour. A lumbar puncture showed an initial pressure of 350 mm of water. The fluid was clear and colorless, and the dynamics normal, the total protein was 75 mg per 100 cc. An electrocardiogram showed a ventricular rate of 80, with normal rhythm, the PR interval was 0.15 second, there was a low T₁ with slight left axis deviation. X-ray study revealed that the heart shadow showed only slight prominence in the region of the left ventricle, the aorta was tortuous but not dilated. The lung fields were clear.

The patient was given up to 3500 cc of fluids daily and a salt poor, low protein (40 gm) diet. In spite of the high fluid intake the daily urinary output ranged from 500 to 800 cc. The blood pressure remained about the same. He began vomiting and the nonprotein nitrogen rose to 90 mg per 100 cc. He quickly went downhill, became comatose and expired on the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR WILFRID J COMEAU The picture which this case presents seems to be one in which the kidneys unquestionably play the dominant role. The heart, although affected, is a secondary factor and of minor significance insofar as the major symptoms are concerned. With regard to the heart you will note that he had had one attack of nocturnal dyspnea, and it is fair I believe, to consider this an attack of left ventricular failure. To go with this he had hypertension, left ventricular enlargement and slight electrocardiographic changes. The attack of dyspnea occurred a week before he died, and I am quite sure that if he had lived long enough the cardiac symptoms would have become more prominent. The x-ray film of his heart shows less enlargement than one might expect but there is some congestion of the hilar shadows, which indicates early pulmonary congestion. The electrocardiogram shows a low, some

times slightly diphasic T₁ and left-axis deviation, the other T waves are of good amplitude. These changes indicate a slight degree of myocardial disease.

Classical symptoms and signs indicate that the kidneys were the primary cause of this man's illness and death. There was marked hypertension with retinopathy and encephalopathy, and in addition there were anemia, urinary findings which are consistent with kidney failure, a high spinal fluid pressure indicating cerebral edema, and finally a rising nonprotein nitrogen with the terminal clinical picture of uremia.

When one makes up his mind that an illness is due to chronic kidney disease and renal failure he is usually presented with an academic problem in differential diagnosis. I say an "academic problem" because the symptoms and signs and treatment of terminal chronic renal disease are more or less identical no matter what the cause may be. One can usually determine whether an individual has chronic kidney disease, but it is often very difficult to decide as to the etiologic background. As a rule, the two things which help most are the history and the clinical course.

In chronic kidney disease one usually considers three etiologic conditions. One is chronic pyelonephritis. It is only within the past few years that people have begun to realize that a former kidney infection such as a pyelitis, is not necessarily a temporary and innocuous condition. Occasionally this initial attack which clears up clinically and is passed off as cured, progresses subclinically to the stage of chronic kidney disease. There is no evidence to indicate such an etiology here.

Chronic glomerulonephritis is a second condition which one considers. Here again the history and course are important in differential diagnosis. In this case there is no history of acute glomerulonephritis, of scarlet fever or of frequent sore throats, and there is no evidence that the patient went through the nephrotic stage of a glomerulonephritis. Hence there is no clue suggesting glomerular nephritis as the etiologic factor.

Third we have benign nephrosclerosis, which is associated with essential hypertension. We do know that he had had hypertension for a year, probably longer. In such cases one generally obtains a history of a long period of hypertension and the level of blood pressure is usually not so high as it was in this case. One can thus see that the differentiation between pyelonephritis, glomerulonephritis and benign nephrosclerosis is very often difficult unless one can get a very

complete history or has a record of the clinical course

In this case, however, there is definite evidence that no one of these three factors, at least clinically, was the cause of his final demise. Here we have a short course, certainly a year, possibly two or three years. There was marked hypertension. The diastolic pressure is very rarely as high as 140 in benign nephrosclerosis. In the three conditions which I have mentioned previously there may be some retinopathy, but rarely however is it as marked as it was in this case, with edema of the disks and evidence of recent and old hemorrhages. It happens that this man took the path of uremia, he might just as well have taken that of heart failure or of a cerebral vascular accident. This particular case presents clinical features which differentiate it very definitely from the three former conditions which I have mentioned, that is, the short course, the marked hypertension, the retinopathy and the death in uremia. We are dealing here, it seems to me, with malignant hypertension. We must remember that malignant hypertension is not necessarily an isolated condition. Occasionally an individual may have glomerulonephritis or pyelonephritis with a superimposed malignant nephrosclerosis. More commonly, however, malignant nephrosclerosis is superimposed on the benign type. There is no doubt in my mind that in this case the diagnosis is malignant hypertension, with malignant nephrosclerosis, possibly superimposed on the benign type, hypertensive heart disease and moderate cardiac enlargement. In addition, there is hypertensive encephalopathy and retinopathy.

DR PAUL D. WHITE: I have nothing to add except to bring up the possibility of small cerebrovascular lesions, which will occur sometimes silently and sometimes with symptoms of headache and eye changes.

DR COMEAU: I might add that I think it is well known, and Dr. Castlemán will probably substantiate me, that arterial changes in benign or malignant hypertension pathologically are not confined to the kidney. Very frequently they are widespread, although the main effect is demonstrated in the kidney.

CLINICAL DIAGNOSES

Chronic glomerulonephritis, with hypertension
Uremia

DR COMEAU'S DIAGNOSES

Malignant arterial hypertension, with malignant nephrosclerosis

Hypertensive heart disease, with moderate cardiac enlargement

Hypertensive encephalopathy and retinopathy
Uremia

ANATOMICAL DIAGNOSES

Chronic vascular nephritis, malignant phase (Uremia)

Cardiac hypertrophy, hypertensive type

Arteriosclerosis, marked, generalized

Bronchopneumonia, bilateral

Pulmonary edema

Infarction of lenticular nucleus and pons

Encephalomalacia, generalized

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMÁN: At autopsy this man showed an enlarged heart, weighing 450 gm., most of the enlargement being due to hypertrophy of the left ventricle. There was no evidence of heart failure. The kidneys weighed 225 gm., being about two thirds their normal weight. On stripping the capsules, we could see a diffuse coarse granularity, the granules being gray with red depressed areas between them—the characteristic appearance of what has been called a malignant vascular nephritis. Histologically, the majority of the arterioles showed marked medial hyalinization with only occasional necrotizing arteriolitis. The larger vessels showed a hyperplastic intimal proliferation. About half the glomeruli showed partial or complete hyalinization.

A few years ago we were convinced that this disease was a specific entity, that is, that nephrosclerosis could be divided into two groups, the benign and the malignant types. Now we believe that these types are probably different phases of the same disease. A patient can certainly go along with benign hypertension for ten years and suddenly develop signs of renal failure and show anatomic changes that may or may not be typical of malignant vascular nephritis. Moritz* has shown very well that necrotizing lesions can be present in the so-called benign type and may be absent in clinically malignant cases. In the brain there were numerous small areas of softening with true infarction in several places, especially in the pons and the lenticular nucleus.

DR WHITE: Were the coronaries involved?

DR CASTLEMÁN: They showed a moderate degree of arteriosclerosis but no occlusion. There were arterial changes in the pancreas and spleen, and a fairly extensive terminal bronchopneumonia was present.

*Moritz, A. R. and Oldt, M. R. Arteriolar sclerosis in hypertensive and non hypertensive individuals. *Am. J. Path.* 13: 679-728, 1937.

The New England Journal of Medicine

Formerly the

Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

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SUBSCRIPTION TERMS: \$6.00 per year in advance, postage paid for the United States; Canada \$7.04 per year; \$8.51 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway Boston, Mass.

HARVEY CUSHING

THE *Journal* has inscribed with a sense of deep regret the death of Harvey Cushing. His removal from our midst permits us the opportunity to record here the debt of gratitude which civilization in general and medicine in particular owe him. The descendant of a long line of doctors (David Cushing, 1768-1814, Cheshire, Massachusetts, Erastus Cushing 1802-1893 Berkshire Medical College, Henry K. Cushing 1827-1910, Cleveland, Ohio), he demonstrated from the beginning an exceptional ambition and ability in our profession. Essentially an aristocrat and a perfectionist, he always evinced the highest sense of obligation to his profession, and if his critical attitude, which tolerated nothing but the best, was difficult for some colleagues from time to time,

it was magnificently good for the world at large. Imbued with great vitality and enormous energy, he became the foremost surgeon of his day, a master-teacher, a profound and prolific investigator, and the most accomplished medical writer in our country.

After a complete training in general surgery largely at the Johns Hopkins Hospital where he fell under the beneficent influence of William Stewart Halsted, Dr. Cushing took up, at his teachers request, the study of the central nervous system as it related to the surgical practice of that day. For the purpose of tilling this field he was equipped with his personal qualities of ambition, intelligence and industry and a technical skill that promised great advances. His contributions to this field gave to medicine the surgical technique requisite for safe exploration of the nervous system and laid down the signposts for the future advancement of knowledge in neurology.

This gift to mankind, however, was but a part of Dr. Cushing's accomplishments. His abiding desire and curiosity to understand completely everything he saw or did led him to become a voracious seeker in medical literature. His intimacy with Sir William Osler quickened and deepened this natural bent into a great love of books. The cultivation of this interest brought about the formation of a great library of the original sources in medicine. He soon became one of the leading medical bibliophiles of his day. But his bibliophilic aspirations were far greater than those of most collectors. In his hands books became really useful; they dropped into the hands of pupils and found their way about. This emphasis and interest in the study of original sources was a major stimulus to his pupils, and not a few men owe their positions and intellectual customs to the habit acquired by this appreciation and love of books.

Naturally Dr. Cushing's explorations, his work and his reading led to new ideas, questions and problems which took him and his pupils and assistants to the laboratory for an answer. His life is an outstanding example of the dictum that work begets ideas. Such great intellectual curiosity and

healthy skepticism led to a series of imposing investigations in experimental surgery and physiology that continuously pushed forward our knowledge of the ductless glands and the central nervous system.

His published articles and books number some three hundred and thirty items. Such voluminous writing bore its undeniable fruit. He became the most accomplished medical writer of his day. Nor to those familiar with his ways did this differ from his technical work or his laboratory investigations. It came through work and his insatiable desire for perfection. No reference was too casual to be neglected or quoted through another's pen or eye—he always saw it himself. The best dictionaries were always at his elbow, and the manuscripts were rewritten and rewritten. In the midst of his busiest years his most revered friend, William Osler, died, and Dr. Cushing gladly assumed the task of writing a biography. In the composition of this masterpiece the same tools and spirit were at work. Files of daily newspapers littered his library for two years, lest any small comment of value be overlooked. There could be no wonder on the part of his intimates when the Pulitzer Prize in Letters was given to him in 1926 for this effort.

Finally and beyond the immense contributions to surgery, science and literature lies the inevitable effect he had on others—his pupils. The brilliance of his works brought young men to him in droves. A casual talk fired the enthusiasm of even the dullards. Once they had secured the opportunity to work with him on his staff the process began. It often started abruptly, it was often difficult, it was never easy. And the education took in all phases. To the beginner, tests which in his mind might have seemed unimportant were magnified, anything in medicine might save life or kill, everything was important and therefore everything had to be perfect, even if it entailed a sleepless night. And it could not be put off. Later in the education came the surgical dressing—it must be neat, it must be comfortable, it might have to be done three times a day. The patient was put in his

proper position—he was everything, anything which made him feel better or more at peace in his mind was good, anything to the contrary was bad. There was no room for in-betweens. Delegation of responsibility was never permitted. "So and so is your patient. You must know all about him, all about his family, if necessary to elicit a proper past history, send for the grandmother, try talking to the patient at night, he might like you better than I." It was a hard row, but it was excellent medicine. In Dr. Cushing's hands, medicine was a religion. His pupils knew this, and although they became very tired and sometimes hurt or angry, the clear light was always there. The "Chief" was right.

But it was not only the technic of handling the patient, it was the proper conduct of a doctor in the sick room. Many an assistant—and it mattered not at all how high in the hierarchy of the hospital system he had climbed—was openly berated for addressing a medical student in front of a patient without the title of doctor. And so it led to the operating room. Here the protection of the patient was complete. His comfort on the operating table was of major importance, and the wound a religious ceremony. It is said that only those who went through the experience can appreciate what it was: there the master surgeon was at his best, and technic was a ritual in which no mistakes could be tolerated. Moreover, these procedures revealed most clearly the dominant spirit of perfection. Five, six and even seven hours of grueling labor were as nothing if the patient might be benefited. And in this effort Dr. Cushing spared himself least of all. No one was ever asked to work harder than he did himself. Very little was said. His example was sufficient. The result of this was seen in all directions, first, the patients recovered, second, his technical procedures were correctly evaluated as works of art. He used instruments as a great violinist uses his bow and was just as careful of them. He left a great heritage to his assistants. He taught them daily the greatest of all truths: that by hard work comes success. Out of this labor, and alone, he built the foundations and

much of the structure of neurological surgery, and in so doing made countless patients happy and useful citizens

It is obvious that Harvey Cushing was an unusual individual, obvious that his driving spirit of perfection coupled with his dynamic energy yielded great fruits. We in New England, the home of his forebears, the happy center where the early part of his formal education took place (Yale College, Harvard Medical School, Massachusetts General Hospital) and the seat where his greatest labors took place (Peter Bent Brigham Hospital), are glad to record here his beneficent influence on the medicine of our time. He has bequeathed to us high principles, and his example in both the art and science of our profession leaves us silent at his feet.

HOW TO CHOOSE YOUR DOCTOR

THIS subject has exercised the thought and ingenuity of many professional and semiprofessional groups, committees on public education and writers of syndicated health columns. In May in a mimeographed statement,* the United States Public Health Service issued another attempt to broadcast such helpful information. The formulas have become rather fixed. The first method advised, that of making inquiry of "your own doctor at your last residence, asking him to recommend a practitioner in the new town to which you are going, is feasible only when circumstances permit the doctor to make a first hand choice, such as that of a personal acquaintance, former classmate or otherwise known person. If such fortuitous circumstances do not exist, apparently one must resort to the directories for information about society memberships, scientific accomplishments and other indirect indices of professional achievement. Lists of such memberships, the possession of which may be presumed to indicate recommendable qualities, are at best cumbersome. As in the Negro spiritual, they provide wheels within wheels. Also as in the song the little wheel goes by Faith but here the smile ends, for the big wheel un-

mistakably goes by the Grace of Scholastic Aptitude

How far can the Grace of Scholastic Aptitude be trusted as a guide to the quality of medical service? To what extent can it be relied on as a measure of judgment, character or professional integrity? The medical schools have been asking themselves these questions for years. They probably have greater misgiving about the answers than any other group within our profession. The medical aptitude test has been devised in an attempt to supply further data. While it has been of considerable aid to those interested in medical education in the appraisal of their future students, the test has on the whole proved to be no more than another measure of general scholastic adaptability, memory or facility of expression. It correlates very closely with the other data collected about prospective students the highest grades of which lead to the conferring of degrees with honors. Yet low-grade scholars have proved themselves capable of becoming high grade doctors. One must conclude that there is no diagnostic test for a "good doctor."

Why not assume that the legal requirements for the practice of medicine are reasonably selective in most places, and let the individual concerned, when he is called on to act make what is known on the diamond as a fielder's choice? If the circumstances in any community are such that this would be a dangerous thing for a newcomer to do, then there exists in that community an extreme public-health emergency. Such emergency needs to be dealt with less by erudition and more by action.

Action of many sorts suggests itself. First the statutory regulations for the practice of medicine should be reviewed. If they are sufficient in authority the spirit of their administration must be scrutinized. If that is above reproach their enforcement needs to be assured. If there still is not a sufficient supply of competent doctors the medical institutions in which they are being trained need attention.

The *Journal* would suggest to anyone in a strange community that the local reputations of its doctors are as trustworthy guides as are those of its bankers, merchants and citizens in general.

**Choosing Your Doctor*. 3 pp. Washington, D. C.: U. S. Public Health Service, 1950.

OBITUARY

GEORGE WASHINGTON
WALES BREWSTER

1866-1939

George Washington Wales Brewster died at his home, 213 Beacon Street, Boston, on September 26, in his seventy-third year. He was born in Roxbury, attended the Roxbury Latin School, and graduated from Harvard College in the class of 1889. After his graduation he attended the Harvard Medical School, graduating from there in 1893. In 1900 he was made surgeon to outpatients at the Massachusetts General Hospital. He served as private assistant to Dr. Maurice Richardson for some years. In 1906 he was made assistant surgeon to the Massachusetts General Hospital, and in 1914 visiting surgeon. In 1927, at the completion of twenty-seven years as a surgeon to this hospital he retired from active service and was appointed to the consulting staff.

Dr. Brewster was a member of many medical and surgical societies, including the Boston Surgical Society, the New England Surgical Society and the American Surgical Association. He was a member of the Tavern Club, The Country Club and the Aesculapian Club.

He is survived by his widow, Ellen Hodge Brewster, and three sons, William, George, Jr., and Henry.

Dr. Brewster was of that school of surgeons who were trained before the days of x-ray and laboratory diagnosis, and throughout his life his judgment of sickness—whether to operate or not—was accurate and sound. Because of his surgical instinct his value as a consultant was great. Dr. Brewster loved to operate, loved surgery and kept up his interest to the very last. His visits to his hospital were a delight and an example to the younger staff members and house officers. At the various meetings in the hospital—surgical, medical and pathological—his cheery presence and sane criticism were always welcome.

Great surgeon and great healer as he was he will be missed most by those who knew him well and who benefited by his loyalty, interest and criticism. His advice was sought by all, and the younger men in particular have suffered a loss that they know can never be filled. Bright, quick, caustic, but always fair he saw through sham and enjoyed exposing it. Instinctively all were drawn to him, and he never failed his friends. Few are the older men who will be honored as he, and great will be anyone who can even partially take his place.

Old people, young people, patients, hospital employees and clubmates will all miss the gruff, but cheery, lovable and distinguished "Old Man."

J V M

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS
AND GYNECOLOGY*

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330 Dartmouth Street
Boston

SEPTIC ABORTION

Mrs. B. G., a twenty-five-year-old primipara, entered the hospital May 25, 1911. Her last regular menstruation had been in February. On May 20, following a fall down stairs, she began to flow and miscarried that night. She continued to flow and to have abdominal pain, the day before entrance she had a chill.

The family history was not obtained. The patient had had no serious illnesses or operations. Catamenia had begun at fourteen, had a twenty-eight-day cycle, and lasted four days, with slight pain at the onset.

Physical examination showed a well-developed and nourished woman with flushed face and a dry, coated tongue. The temperature was 102°F., the pulse 120 and of good quality. The breasts were enlarged and somewhat congested. The heart sounds were clear and regular. The lungs were clear and resonant throughout. The abdomen was tender in both lower quadrants, but there was no spasm. The uterus was enlarged to the size of a two-months' pregnancy and was soft, symmetrical and non-tender. There was a slight blood-tinged discharge. The vaults were soft and slightly tender, but no masses were felt.

The white-blood-cell count was 16,000, the hemoglobin 75 per cent. The urine was high colored, with a specific gravity of 1.024, a slightest possible trace of albumin and no sugar. The sediment showed red, white and squamous epithelial cells in large numbers.

The patient was kept under observation for twenty-four hours, but as there was no improvement the following day, the cervix was dilated sufficiently under light anesthesia to introduce a finger into the uterus. No embryonic remains were found, and a gauze strip saturated with tincture of iodine was placed in the uterine cavity and left there for six hours.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

The patient was given hot vaginal douches of boric solution daily and placed out-of-doors. For nine days after entrance the temperature ranged from 101 to 104°F., and the pulse from 100 to 128, the average being between 110 and 120. On the tenth day the temperature abruptly came down to normal and remained so until discharge.

Discharge examination showed the uterus to be normal in size and slightly retroverted, the vaults were negative. The patient left the hospital on June 12.

Comment The treatment of this case represents unusual conservatism for the year 1911. Some men at that date made curettage a routine procedure in septic abortion. We have learned that this is harmful, today the treatment would have been even more conservative. In the absence of actual bleeding the uterus would not have been invaded except for the purpose of getting a culture, and blood cultures would also have been obtained, if one or both of these cultures had been positive, chemotherapy might have been instituted. The use of antiseptics in the uterine cavity has proved of no value. This patient recovered when her powers of resistance improved sufficiently to overcome the infection. The outdoor treatment undoubtedly helped.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions, given by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau have been arranged for the week beginning October 23.

BAKENEABLE

Sunday October 29 at 4:00 p.m., at the Cape Cod Hospital, Hyannis. Subject—The Use of Drugs in the Treatment of Childhood Infections. Instructor Charles F. McKhann. Donald E. Higgins, *Chairman*.

BRISTOL NORTH

Thursday October 26, at 4:00 p.m., at the Morton Hospital, Taunton. Subject—Syphilis in Pregnancy and the Offspring. Instructor Francis M. Thurmon. Lester E. Butler, *Chairman*.

BRISTOL SOUTH (New Bedford Section)

Friday October 27 at 4:00 p.m., at St. Luke's Hospital, New Bedford. Subject—The Use of Biological Preparations in Pediatric Practice. Instructor: Louis K. Diamond. Robert H. Goodwin, *Chairman*.

EMPEX NORTH

Friday October 27 at 4:30 p.m., at the Lawrence General Hospital, Lawrence. Subject—Gonorrhea in the Female. Instructor Alonzo K. Paine. John Parr, *Chairman*.

EMPEX SOUTH

Tuesday October 24 at 4:00 p.m., in the Conference Room of the Salem Hospital, Salem. Subject—Pneumonia. Instructor W. Barry Wood, Jr. J. Robert Shaughnessy, *Chairman*.

MIDDLESEX EAST

Tuesday, October 24 at 4:00 p.m., at the Melrose Hospital, Melrose. Subject—Common Problems of Neurology. Indications for lumbar puncture. Instructor H. Houston Merritt. Walter H. Flanders, *Chairman*.

MIDDLESEX NORTH

Friday October 27 at 4:45 p.m., at St. John's Hospital, Lowell. Subject—Indications for Cesarean Section. Instructor Robert L. DeNormandie. William S. Lawler, *Chairman*.

WORCESTER DISTRICT (Milford Section)

Tuesday October 24 at 3:30 p.m., in the Nurses Home of the Milford Hospital, Milford. Subject—Gonorrhea in the Female. Instructor Oscar F. Cox, Jr. Joseph Ashkins, *Chairman*.

WORCESTER DISTRICT (Worcester Section)

Friday October 27 at 8:00 p.m., in the Staff Room of the Worcester City Hospital, Worcester. Subject—Cardiovascular Disease. Eleven important questions about heart disease and their answers. Instructor Sylvester McGinn. George C. Tully, *Chairman*.

WORCESTER NORTH DISTRICT

Friday October 27, at 4:30 p.m., in the Nurses Home of the Burbank Hospital, Fitchburg. Subject—The Use of Biological Preparations in Pediatric Practice. Instructor Warren R. Sisson. George P. Keavey, *Chairman*.

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Royal College of Physicians and Surgeons, London,
1934
- AUFBRANG, OTTO E., 60 Egmont Street, Brookline.
Harvard Medical School 1934
- BEIOELMAN, HERMAN, 23 Waumbek Street, Roxbury.
Tufts College Medical School 1937
- BRENNER, CHARLES, 185 Winthrop Road, Brookline.
Harvard Medical School 1935
- BRINES, JOHN K., 29 Martin Road, Wellesley.
Harvard Medical School 1936.
- BROOKS, OSCAR D., 401 Boylston Street, Brookline.
Middlesex College of Medicine and Surgery 1930
- BUSH, CHARLES W., JR., 293 Eliot Street, Milton.
Boston University School of Medicine 1936.
- CHEEVER, FRANCIS S., 828 Washington Street, Wellesley.
Harvard Medical School 1936.
- COHEN, JACK D., 10 Fuller Street, Brookline.
Tufts College Medical School 1937
- COLCOCK, BENTLEY P., 50 Jamaica Way, Jamaica Plain.
University of Pennsylvania School of Medicine, 1933

DICKSON, ELLSWORTH J. M., 888 Great Plain Avenue, Needham
Tufts College Medical School, 1912

DYNES, JOHN B., 11 Tetlow Street, Boston (Roxbury)
Harvard Medical School, 1932

FORBES, ANNE P., 3041 Adams Street, Milton
Columbia University, College of Physicians and Surgeons, 1936

FROMER, JOHN L., 62 Marion Street, Brookline.
New York University College of Medicine, 1932

GIDDON, ELLIOT D., 77 Gibbs Street, Brookline
Boston University School of Medicine, 1936

GROSSMAN, SAMUEL, 32 Wenonah Street, Roxbury
Kansas City University of Physicians and Surgeons, 1932.

HISCOCK, MABELLE C., New England Hospital for Women and Children, Roxbury
Johns Hopkins University School of Medicine, 1935

HOOPER, LANGDON, 51 Clovelly Road, Wellesley Hills
Harvard Medical School, 1937

HUBER, WILLIAM McP., 1863 Beacon Street, Brookline
University of Pennsylvania School of Medicine, 1930

LAMB, GORDON R., 144 Grove Street, Brookline.
University of Michigan Medical School, 1933

LATHROP, FRANK D., 144 Grove Street, Brookline
University of Michigan Medical School, 1934

LINDBERG, THEODORE F., 591 Morton Street, Dorchester Center
Northwestern University Medical School, 1930

MORIARTY, JAMES E., 1074 South Street, Roslindale.
Middlesex College of Medicine and Surgery, 1933

MORSE, FRANK P., JR., 2 Perkins Manor, Perkins Street, Jamaica Plain.
Tufts College Medical School, 1936

NICHOLSON, MORRIS J., 306 Riverway, Roxbury
University of Maryland School of Medicine, 1936

REUTER, ROBERT J., 370 Longwood Avenue, Boston (Roxbury)
Marquette University School of Medicine, 1936

ROMANO, JOHN, 333 Longwood Avenue, Boston (Roxbury)
Marquette University School of Medicine, 1934

SALTER, WILLIAM T., 1 Lancaster Lane, Milton
Harvard Medical School, 1925

SCHULTZ, PHILIP E., 370 Longwood Avenue, Boston, (Roxbury)
Creighton University School of Medicine, 1933

SILBERT, NATHAN E., 12 Wildwood Street, Dorchester
Kansas City University of Physicians and Surgeons, 1933

SODERS, CARLTON R., 50 Jamaicaaway, Jamaica Plain
Harvard Medical School, 1933

STAPLES O. SIERWIN, 136 Milton Avenue, Hyde Park
Harvard Medical School, 1935

THORNTON, JOSEPH P., 87 Adams Street, Dorchester
Boston University School of Medicine, 1936

VASTINE, MARY F., 329 Longwood Avenue, Boston, (Roxbury)
Woman's Medical College of Pennsylvania, 1934

WAGNER, RICHARD, 197 Longwood Avenue, Brookline
Medical Faculty of the University of Vienna, 1912

WEKSTEIN ABRAHAM J., 1331 Blue Hill Avenue, Mattapan
Middlesex College of Medicine and Surgery, 1934

WEXLER, JACOB, 967 Blue Hill Avenue, Dorchester
Middlesex College of Medicine and Surgery, 1935

ZALVAN, JACOB, 175 Exchange Street, Mills
Middlesex College of Medicine and Surgery, 1935

Frank S. Cruickshank, *Secretary*

NORFOLK SOUTH DISTRICT

CHIMINELLO, FRANK J., 18 Vine Avenue, Quincy
Boston University School of Medicine, 1939

FRANKMAN, WILLIAM, 736 Hancock Street, Quincy
St. Louis College of Physicians and Surgeons, 1937

PHILBROOK, F. RANDOLF, 528 North Main Street, Ranc
Boston University School of Medicine, 1935

SARGENT, MORGAN, 24 Whitney Road, Quincy
Yale University School of Medicine, 1937

SLEMONS, MARION L., 29 Greenleaf Street, Quincy
University of Michigan Medical School, 1936

Robert L. Cook, *Secretary*

PLYMOUTH DISTRICT

BERGMAN, MACKS L., State Farm
University of Vermont College of Medicine, 1937

LUDLOW, WILLIAM V., 4 Jericho Road, Scituate.
Tufts College Medical School, 1937

MACLAUGHLIN, CHARLES H., State Farm
Tufts College Medical School, 1936

WASSERMAN, MITCHELL, 42 South Main Street, Marsh
Boston University School of Medicine, 1936

Howard C. Reed, *Secretary*

SUFFOLK DISTRICT

COGGESHALL, HOWARD C., 10 Pinckney Street, Boston
Indiana University School of Medicine, 1932

COHEN, SAMUEL L., 44 Phillips Street, Boston
Boston University School of Medicine, 1937

DEVINE, JOSEPH W., 773 Broadway, South Boston
College of Physicians and Surgeons, Boston, 1935

DERHAGOPIAN, ARDASHES P., 35 Crescent Avenue, Ch
Tufts College Medical School, 1937

ELIA, ANDREW D., 362 Commonwealth Avenue, Bost
Boston University School of Medicine, 1935

FROTHINGHAM, JOSEPH R., 157 Bay State Road, Bosto
Harvard Medical School, 1937

HIRSCH, OSKAR, 400 Commonwealth Avenue, Boston
Vienna University, 1902

HYMAN, MAYER, The Myles Standish, Beacon S
Boston
Rush Medical College of the University of Chi
1937

KUNKEL, PAUL, Boston City Hospital, Boston
Washington University School of Medicine, 1937

LINDEMANN, ERICH, 222 Beacon Street, Boston
University of Giessen, 1924

MANGANELLI, CHARLES V., 110 Marginal Street, East B
Tufts College Medical School, 1938

ROIFF, HARRY S., 159 Shurtleff Street, Chelsea.
St. Louis College of Physicians and Surgeons, 1937

SEWALL, KENNETH W., 64 Charlesgate East, Boston
Harvard Medical School, 1934

WARREN RICHARD 112 Beacon Street, Boston.

Harvard Medical School 1934

WIENER, HARRY J., 51 Nahant Avenue, Revere.

University of Michigan Medical School, 1936

M. Henry Clifford *Secretary*

WORCESTER DISTRICT

CARLETON THOMAS M., West Main Street, Brookfield.

Tufts College Medical School 1938

CONSTANTIN HAROLD M., 39 Burdett Street, Worcester

Long Island College of Medicine, 1937

FULDER, HANS, 10 Cottage Street, Worcester

University of Lausanne, Switzerland Medical School 1934

GARIFFY ALONZO J. A., Summer Street, Barre.

Tufts College Medical School 1935

GRAINGER, JAMES E., 981 Pleasant Street, Worcester

Tufts College Medical School 1938

HADDAD, ARTHUR K., Worcester City Hospital Worcester

Tufts College Medical School 1937

LINTINO JOSEPH W. 85 Walnut Street, Clinton.

Royal University of Rome Medical School 1934

REMY SYLVIO B., 3 May Street, Webster

Georgetown University School of Medicine, 1937

ROSENBLUM HARRY A., Fiskdale.

Kansas City University of Physicians and Surgeons, 1932.

SOOLA JOSEPH A., 508 Salisbury Street, Worcester

Middlesex College of Medicine and Surgery 1931

George C. Tully *Secretary*

WORCESTER NORTH DISTRICT

BRINZGAR WILLARD C. Gardner State Hospital East Gardner

University of Nebraska College of Medicine, 1937

BROMSON BENJAMIN 137 Marble Street, Athol.

Middlesex College of Medicine and Surgery 1925

GROSSMAN MYER J., 599 Main Street, Athol.

Middlesex College of Medicine and Surgery 1933

LAPIERRE, J. CHARLES 21 Waverly Street, Fitchburg

University of Montreal Faculty of Medicine, 1922.

MATTLA, ANTHONY F., 97 Summer Street, Fitchburg

College of Physicians and Surgeons, Boston 1921

SILVER, JOSEPH M., 46 Prichard Street, Fitchburg.

Middlesex College of Medicine and Surgery 1933.

WASSER, LOUIS, Elm Street, Baldwinsville.

Middlesex College of Medicine and Surgery 1933.

Edward A. Adams, *Secretary*

DEATHS

DOHERTY—HENRY L. DOHERTY M.D., of Stoughton, died October 9. He was in his forty sixth year.

Born in Stoneliam he attended Boston College and received his degree from the Harvard Medical School in 1920. He started practice in Stoughton in 1922. Dr. Doherty was a director of the Stoughton Hospital and associate physician at the Norwood Hospital. He held

memberships in the Massachusetts Medical Society and the American Medical Association.

His widow a daughter and three sons survive him.

LEARY—WILLIAM C. LEARY M.D., of Springfield died October 13. He was in his seventy-first year.

Dr. Leary attended Holy Cross College and received his degree from the Bellevue Hospital Medical College in 1894.

He was a fellow of the Massachusetts Medical Society and the American Medical Association and was on the staff of the Mercy Hospital Springfield.

GREEN LIGHTS TO HEALTH

OCTOBER—NOVEMBER—DECEMBER

SPONSORED BY THE MASSACHUSETTS MEDICAL SOCIETY AND THE MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COURTESY WAAS—WEDNESDAYS, 4:00 P.M.

October 25 National Hearing Week. Philip E. Meltzer

November 1 Care of the Eyes. Walter B. Lancaster

November 8 Heart Disease in Middle Life. Howard B.

Spargue.

November 15 Indigestion and How to Treat It. Edward S. Emery Jr.

November 22 Varicose Veins. Reginald H. Smithwick.

November 29 High Blood Pressure. Robert S. Palmer

December 6 The Family Physician. David Cheever

December 13 Nervous Fatigue. Kenneth J. Tillotson.

December 20 Hygiene of the Digestive Tract. Allen G. Brailey

December 27 Hospitals. Nathaniel W. Faxon.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

ALLEN—WALTER A. ALLEN M.D., of Hampstead died suddenly at Haverhill Massachusetts on August 23.

Dr. Allen was born on January 10 1869 in Boston the son of George Allen and Sarah Ann (Collins) Allen, of Hampstead. He graduated in 1889 from Phillips Exeter Academy and in 1892 from Dartmouth Medical School.

He served on the Hampstead School Board for three years and for many years was on the Board of Health. He was chosen representative for two terms and was a state senator in 1905 and 1906. Dr. Allen was a member of the American Medical Association, of the New Hampshire, Rockingham County and Pentucket medical societies and of the Haverhill Medical Club. During the World War he served in the U. S. Army Medical Corps with the rank of captain.

Dr. Allen is survived by his widow Mrs. Grace A. Allen.

HENRY H. AMESDEN *Necrologist*
New Hampshire Medical Society

VERMONT STATE MEDICAL SOCIETY

UNIVERSITY OF VERMONT COLLEGE OF MEDICINE NAMES NEW DEAN

The appointment of one of the youngest deans to one of the oldest medical colleges in the United States was recently officially approved by vote of the Board of Trustees of the University of Vermont. The appointee, Dr.

Hardy Alfred Kemp, who has already entered on his new duties, was formerly in charge of the Department of Bacteriology, Hygiene and Preventive Medicine at Baylor University College of Medicine, Dallas, Texas. Born July 13, 1902, at Monett, Missouri, he is just over thirty-seven years old. The University of Vermont College of Medicine is the sixth oldest institution of its kind in the United States. Dean Kemp is perhaps the youngest of medical college deans. Women were first admitted to the college in 1920. The medical curriculum was extensively reorganized in 1937. Since the death of the former dean, Dr. J. N. Jenne, two years ago, the affairs of the institution have been conducted by a committee.

Dean Kemp is perhaps best known for his researches on endemic typhus fever and relapsing fever. In 1934 he won the first award from the Southern Medical Association for his study of relapsing fever. Dean Kemp's work with these two diseases included epidemiological and clinical studies and the development of diagnostic tests.

He received his medical education from St. Louis University School of Medicine, taking his degree in 1926. His internship was spent at the William Beaumont General Hospital, El Paso, Texas.

After a year of private practice at Aurora, Missouri, Dean Kemp spent four months as pathologist in the Missouri State Hospital Service, having charge of the laboratories at the Missouri State Sanatorium at Mt. Vernon. In the fall of 1928 he accepted the associate professorship of bacteriology and hygiene at Baylor University College of Medicine and became full professor in 1937. He was visiting professor of bacteriology at the University of Texas Graduate School, Austin, Texas, during the summer sessions of 1935, 1936, 1937 and 1938, teaching immunology. As lecturer at the Southwestern Institute for Social Workers, under the auspices of the Civic Federations of Dallas and various state and federal agencies, during the winters of 1935, 1936, and 1937 he taught preventive medicine and public-health law.

Dean Kemp is a major in the Medical Reserve Corps of the U. S. Army.

CHANGES IN TEACHING POLICY

Dean Hardy A. Kemp of the medical college of the University of Vermont College of Medicine, speaking recently before members of the Washington County Medical Society, told of some of the changes being instituted in the instruction program of the school.

Among the teaching practices being discontinued are those of preceptorship and undergraduate internships in hospitals throughout the State. For a number of years seniors have been sent out as a part of their instructional program to work with resident physicians in various parts of the State, the idea being to give them practical experience in their coming profession; they also served undergraduate internships in many of the hospitals of the State. This practice will be discontinued, and the work in the state institutions at Waterbury and Pittsford will be curtailed.

Dean Kemp stated that it was with some reluctance that the work was being dropped, but that its discontinuance was necessitated in order to consolidate the work of the students at the college.

Some of the student work being added to the program is a month of obstetric training at the Wesson Maternity Hospital, Springfield, Massachusetts, and a month of urology at the Worcester City Hospital, Worcester, Massachusetts. Arrangements have also been completed, said Dean Kemp, for the full use of clinical facilities at the

DeGoesbriand Hospital in Burlington and the Fanny Allen Hospital at Winooski Park.

MISCELLANY

MAINE NEWS

MAINE MEDICAL ASSOCIATION

The fall clinical session of the Maine Medical Association will be held at Waterville on October 25 and 26. Headquarters and registration will be at the Elmwood Hotel. The clinics will be held from 9:30 a.m. to 3:30 p.m. at the Central Maine Sanatorium in Fairfield and the Elm City Hospital, Sisters Hospital and Thayer Hospital in Waterville. Dinners and evening meetings will be held at the Elmwood Hotel. The various clinics will be in the nature of dry clinics, ward rounds and demonstrations of cases and x-rays.

Of especial importance are the two evening programs, which have been arranged by the Committee on Graduate Education. Wednesday evening, October 25, there will be a panel discussion on anesthesia. Dr. Howard M. Clute, of Boston, will discuss the subject from the point of view of the surgeon, Dr. M. Fletcher Eades, of Boston, will take up the subject of anesthesia and analgesia in obstetrics, Dr. Sidney C. Wiggins, of Boston, will discuss the general subject, Dr. Gilbert Clapperton, of Lewiston, will speak on the subject from the viewpoint of the small general hospital, and Dr. Paluel J. Flagg, of New York City, will discuss intratracheal anesthesia and asphyxia and will summarize the whole discussion. The evening program for Thursday, October 26, will be held under the auspices of the Kennebec County Medical Association, with Dr. Elliott C. Joslin, of Boston, as speaker.

NOTICES

REMOVAL

JOSEPH D. FERRONE, M.D., announces the removal of his office to 99 Bay State Road, Boston.

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic of the Peter Bent Brigham Hospital will be held on Wednesday afternoon, October 25, at 2:00. Drs. Robert M. Zollinger and Soma Weiss will speak on "Vomiting." A clinicopathological conference, conducted by Dr. Elliott C. Cutler, will follow.

On Thursday morning, October 26, at 8:30, there will be a combined clinic of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, held at the Children's Hospital. Dr. Frank R. Ober will conduct.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER, M.D., *Secretary*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday, October 24, in the amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance), at 8:15 p.m. Dr. Soma Weiss will preside.

PROGRAM

Presentation of Cases

Pseudohemoglobin and Related Compounds in Health and Disease. Dr. Otto Shales

Medical students and physicians are cordially invited to attend.

ROBERT M. ZOLLINGER, M.D., *Secretary*

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday evening November 7 at 8 15

Dr Morris Fishbein editor of the *Journal of the American Medical Association* will speak on "American Medicine and the National Government."

DAVID B STEARNS, M.D., Secretary

BOSTON DOCTORS SYMPHONY ORCHESTRA



The Boston Doctors Symphony Orchestra will rehearse under Alexander Theide, former concert master with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, two Thurs-

days at 8.30 p.m., beginning October 19 in Studio A Station WMEX, 70 Brookline Avenue Boston. Those interested in becoming members should communicate with Dr Julius Loman, Pelham Hall Hotel Brookline (BEA 2430)

MASSACHUSETTS GENERAL HOSPITAL

The next Hospital Research Meeting will be held in the Ether Dome of the Massachusetts General Hospital on Tuesday October 31 at 5:00 p.m.

PROGRAM

Menopausal Osteoporosis. Dr Fuller Albright, Miss Esther Bloomberg Drs. P. H. Smith and H. W. Sulkowitch

Factors Influencing Ability of Solutions to Dissolve Calcium-Phosphate Structures. Drs. H. W. Sulkowitch, Fuller Albright and Max Rosenheim and Miss Robina Murdock.

Assays of 17 keto-Sterones in Endocrine Diagnoses and Interpretations. Drs. Russell Fraser Ann Forbes and Fuller Albright.

HENRY K. BEECHER M.D. Secretary

NORFOLK DISTRICT MEDICAL SOCIETY

The next meeting of the Norfolk District Medical Society will be held to St. Elizabeth's Hospital Brighton on Tuesday evening October 24 at 8 15

PROGRAM

Moving Pictures of the Reconstruction of a Hand. Dr Thomas F. Broderick.

Medicine and the Law. Dr John J. Downing

Case Presentations Problems in diagnosis. Dr William T. O'Halloran.

Endocrinology in Relation to Menstrual Disturbances. Dr Edward L. Kuckham.

FRANK CRUICKSHANK, M.D., Secretary

MASSACHUSETTS ITALIAN MEDICAL SOCIETY

The regular meeting of the Massachusetts Italian Medical Society will be held at the Hotel Kenmore, Boston on Friday evening October 27 at 9:00 Dr Robert Zollinger will speak on "Surgical Aspects of Peptic Ulcers. Includ-

ing diagnosis and treatment" (lantern slides) A general discussion will follow.

The medical profession is cordially invited to attend

CARL F. MARALDI, M.D., Secretary

MASSACHUSETTS PUBLIC HEALTH ASSOCIATION

The October meeting of the Massachusetts Public Health Association will be held Thursday October 26, at the University Club Boston.

SECTION MEETINGS—10 45 A.M.

BOARD OF HEALTH SECTION

Symposium on Health and National Defense.

Viewpoint of the Health Officer John E. Gordon M.D.

Viewpoint of the Public Health Engineer Arthur D. Weston C.E.

Viewpoint of the Public Health Nurse. Sophie C. Nelson, R.N.

LABORATORY SECTION

Trichinosis Donald L. Augustine, Sc.D.

The Uses of Blood Grouping William C. Boyd Ph.D.

Use of Placental Blood for Transfusions (colored motion pictures) Frank E. Barton M.D. Boston

CHILD HEALTH SECTION

The Child The influence of economic factors. Subject introduced by Miss Charlotte Raymond Community Nutritionist, Newton

Discussants Dr Harold W. Stevens health officer (leader)

Miss Grace Lawrence, nurse.

Mrs. Albert Hutchinson, lay representative.

Miss Mary Spalding nutritionist.

Miss Harnet Parsons, social worker

Miss Mary Pfaffmann health educator

LUNCHEON AND MEETING—1:00 P.M.

Implications of the War in Europe on Public Health in the United States. Frederick F. Russell M.D.

NEW ENGLAND MEDICAL CENTER

During the week of November 6-11 a series of teaching clinics on cancer will be held at the Boston Dispensary The schedule is as follows

MONDAY NOVEMBER 6

MORNING. Symposium on Oral Cancer

Dr Richard H. Norton Jr. Oral Cancer Prophylaxis

Dr Kurt H. Thoma Oral Cancer (exclusive of tongue and lip)

Dr Roy E. Mabrey Carcinoma of Tongue and Lip

AFTERNOON. Symposium on Cancer of the Stomach.

Dr Katherine S. Andrews Diagnosis

Dr Jacob Schloss Gastroscopy

Dr Walter E. Garrey Peritoneoscopy

Dr Alice Ettinger Ray

Dr Arthur W. Allen Surgery

Dr H. Edward MacMahon Pathology

THURSDAY NOVEMBER 9

MORNING. Discussion of Carcinoma of the Large Bowel and of Gynecological Cancer

Dr Louis E. Phaneuf Gynecological Cancer
 Dr H Edward MacMahon Gynecological Cancer, Pathology
 Dr William M. Shedden Cancer of Large Bowel and Rectum (motion pictures)

AFTERNOON Teaching Clinics on Breast and Bone Tumors

Dr Paul R. Hinchey Breast Tumors
 Dr Edward A. Cooney Breast Cancer
 Dr Thomas H. Peterson and Dr John D. Adams Bone Tumors

FRIDAY NOVEMBER 10

MORNING Clinic on Hodgkin's Disease.

Dr William Dameshek and Dr Isadore Olef Hodgkin's Disease.
 Dr H Edward MacMahon Pathology of Hodgkin's Disease.

SATURDAY, NOVEMBER 11

MORNING Symposium on Intrathoracic Cancer

Dr Richard H. Overholt Lung Cancer
 Dr Reeve H. Betts Bronchoscopy
 Dr H Edward MacMahon Pathology of Intrathoracic Cancer

These clinics are sponsored by the Massachusetts Department of Public Health. They are given without charge, but admission will be by ticket, as the number to be admitted is limited.

Luncheon may be procured at the cafeteria of the New England Medical Center.

If you plan to attend one or more of these teaching clinics, please notify Chairman, Postgraduate Division, Tufts College Medical School, 30 Bennet Street, Boston, Mass.

ANNUAL AWARDS OF THE NEW ENGLAND SOCIETY OF PSYCHIATRY

To encourage the young medical workers in New England in the field of psychiatry to undertake scientific work and to publish the results of it, the New England Society of Psychiatry offers two awards, one of fifty dollars and one of twenty-five dollars, for the two best papers published during the calendar year of 1939. The papers shall be judged on the basis of their scientific quality by a special examining committee and the Executive Committee of the New England Society of Psychiatry.

The awards will be made and announced at the spring meeting of the New England Society of Psychiatry. Writers who have once received an award are not again eligible. Applicants should send reprints of articles or the journal in which articles appear before March 1, 1940, to the secretary, Dr George A. Elliott (Connecticut State Hospital, Middletown, Connecticut).

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, OCTOBER 23

TUESDAY OCTOBER 24

- 9-10 a.m. Endocrine Clinic Dr C. H. Lawrence. Joseph H. Pratt Diagnostic Hospital
- *10 a.m.-12 30 p.m. Boston Dispensary tumor clinic
- *11 15 p.m. Norfolk District Medical Society St. Elizabeth's Hospital
- *11 15 p.m. Harvard Medical Society Amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance)

WEDNESDAY OCTOBER 25

- *9-10 a.m. Hospital case presentation Dr S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital
- *12 m. Clinicopathological conference Children's Hospital Amphitheater
- *2 p.m. Joint medical and surgical clinic Peter Bent Brigham Hospital
- *6 p.m. Metropolitan District Dental Society Hotel Vendome Boston

THURSDAY OCTOBER 26

- *8 30 a.m. Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital at the Children's Hospital
- *9-10 a.m. Ventricular Fibrillation as the Mechanism of Sudden Death in Patients with Coronary Occlusion Dr Henry Miller Joseph H. Pratt Diagnostic Hospital
- 10 45 a.m. Massachusetts Public Health Association University Club Boston

FRIDAY OCTOBER 27

- *9-10 a.m. Pulmonary Embolism and Infarction Dr A. O. Hampton Joseph H. Pratt Diagnostic Hospital
- *10 a.m.-12 30 p.m. Boston Dispensary tumor clinic.
- *9 p.m. Massachusetts Italian Medical Society Hotel Kenmore, Boston

SATURDAY OCTOBER 28

- *9-10 a.m. Hospital case presentation Dr S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital
- *10 a.m.-12 m. Medical staff rounds of the Peter Bent Brigham Hospital Conducted by Dr C. Sidney Burwell
- *Open to the medical profession

OCTOBER 20 — Boston Dispensary Luncheon meeting of the clinical staff Page 589 issue of October 12

OCTOBER 23—NOVEMBER 3 — New York Academy of Medicine. Page 97 issue of June 8

OCTOBER 24 — Harvard Medical Society Page 632

OCTOBER 25 — Peter Bent Brigham Hospital Joint medical and surgical clinic Page 632

OCTOBER 25 — Metropolitan District Dental Society Page 544 issue of October 5

OCTOBER 26 — Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital Page 632

OCTOBER 26 — Massachusetts Public Health Association Page 633

OCTOBER 27 — Massachusetts Italian Medical Society Page 633

OCTOBER 30 — New England Heart Association Page 589 issue of October 12

OCTOBER 31 — Massachusetts General Hospital Research meeting Page 633

NOVEMBER 6-11 — New England Medical Center Teaching Clinics Cancer Page 633

NOVEMBER 7 — Greater Boston Medical Society Page 633

NOVEMBER 8 9 — New England Society of Physical Medicine in conjunction with the Academy of Physical Medicine Hotel Kenmore Boston. Program to be announced

NOVEMBER 9 — Pentucket Association of Physicians 8 30 p.m. Hotel Bartlett Haverhill

DECEMBER 2 — American Board of Obstetrics and Gynecology Page 10 issue of June 15

JANUARY 6 JUNE 8-11 1940 — American Board of Obstetrics and Gynecology Page 160 issue of July 27

JANUARY 22-25 1940 — American Academy of Orthopaedic Surgeons Hotel Statler Boston

MARCH 7-9 1940 — The New England Hospital Association Hotel Statler Boston

MAY 14 1940 — Pharmacopocical Convention Page 894 issue of May 25

JUNE 7-9 1940 — American Board of Obstetrics and Gynecology Page 1019 issue of June 15

DISTRICT MEDICAL SOCIETIES

NORFOLK

OCTOBER 24 — Page 633

SUFFOLK

OCTOBER 25 — Page 546 issue of October 5

NOVEMBER 29 — Censors meeting Page 441 issue of September 14

NOVEMBER 29 — Scientific meeting Treatment of Syphilis Dr Harold Hyman Dr Louis Chargin and Dr William Leifer of New York City

JANUARY 31 1940 — Scientific meeting Subject to be announced later

MARCH 27 — Scientific meeting Symposium on Ulcerative Colitis and Diarrhea Under the direction of Dr Chester M. Jones

APRIL 24 — Annual meeting in conjunction with the Boston Medical Library Election of officers Program and speakers to be announced later

The New England Journal of Medicine

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VOLUME 221

OCTOBER 26, 1939

NUMBER 17

THE ANTERIOR PITUITARY GLAND AND DIABETES MELLITUS*

FRANK G YOUNG†

LONDON ENGLAND

OUR knowledge of the influence of the pituitary gland on carbohydrate metabolism, unsatisfactory though it may be, has increased with remarkable rapidity during the last ten years. It will be universally agreed that the credit for the initiation of this rapid advance in our knowledge should go to Houssay and his colleagues in Buenos Aires, the important pioneer investigations of this group of workers opened up an entirely new field of research, a field that has yielded results of the greatest importance in the formulation of our present theories of carbohydrate metabolism. Striking developments have since been made in other laboratories, of which must be mentioned the investigations of Long, Lukens and their collaborators on the role of the adrenal cortex in experimental diabetes, the researches of Russell Cori, Bennett and others on the nature of the metabolism of the hypophysectomized animals and the significant investigations of Collip, H M Evans, Himsforth, Soskin and others.

The numerous publications of Houssay and his collaborators have been adequately reviewed during the last few years (Houssay, 1936 and 1937) and no more will be done here than to summarize their fundamentally important initial results. These can be conveniently considered under five main headings:

(1) Experimental removal of the pituitary gland results in greatly increased sensitivity to the hypoglycemic action of insulin (Houssay and Magenta).

(2) In toads, removal of the pars glandularis of the hypophysis, as well as of the whole pituitary gland, greatly increases the sensitivity of the animal to the action of insulin. The hypersensitivity of the hypophysectomized toad to the action of insulin could be diminished by treatment with preparations from the pars glandularis of the pituitary gland, although preparations from the pars

nervosa together with the pars intermedia were ineffective under similar conditions (Houssay and Potick). Similar results with respect to the importance of the anterior lobe in the control of insulin sensitivity have since been obtained with rats by other workers (Pencharz, Cori and Russell, Swann and Fitzgerald), although Geisinger Campbell and Ishikawa had previously found that in one dog extirpation of the anterior lobe of the pituitary gland was not followed by a great increase in insulin sensitivity such as follows removal of the whole gland.

(3) In toads and dogs, hypophysectomy previous to or following pancreatectomy usually diminishes the severity of the diabetic condition which results from removal of the pancreas only, in these species (Houssay and Biasotti).

(4) Treatment of hypophysectomized and depancreatized animals with anterior pituitary extracts results in a great intensification of the diabetic condition, indicating the possibility that in animals from which the pancreas alone is removed, the diabetic condition is brought to its normal degree of intensity under the influence of the secretions of the pituitary gland (Houssay and Biasotti, Houssay, 1936).

(5) The injection of suitable anterior pituitary extracts into normal animals results in the appearance of symptoms of diabetes (Houssay Biasotti and Rietti). In this observation Houssay and his colleagues were anticipated by two other groups of workers (H M Evans et al., and Baumann and Marine). In the experiments of Evans and his colleagues a diabetic condition was observed in two dogs eight or nine months after daily injections of an anterior pituitary growth promoting extract had been instituted. The animals were in a poor condition at this time and the diabetic condition did not disappear for some months after cessation of treatment, although in the experiments of Houssay and others the symptoms subsided and disap-

*From the National Institute for Medical Research, London. E gland.
†This paper was delivered in part as a lecture at the Harvard Medical School on April 20, 1939.
†Fellow of the Medical Research Council National Institute for Medical Research.

peared within a few days of stopping daily injections of extract

These observations by Houssay and others suggested, in agreement with the earlier clinical observations, that overactivity of the pituitary gland, as well as dysfunction of the islets of Langerhans of the pancreas, might be considered as a possible cause of diabetes mellitus. Houssay's results stressed the importance in carbohydrate metabolism of the anterior lobe, rather than that of the posterior portion of the pituitary gland, and although Collip has recently suggested that the

THE DIABETOGENIC ACTION OF CRUDE ANTERIOR PITUITARY EXTRACT

When an animal receives one or more daily injections of anterior pituitary extract, it may sub-

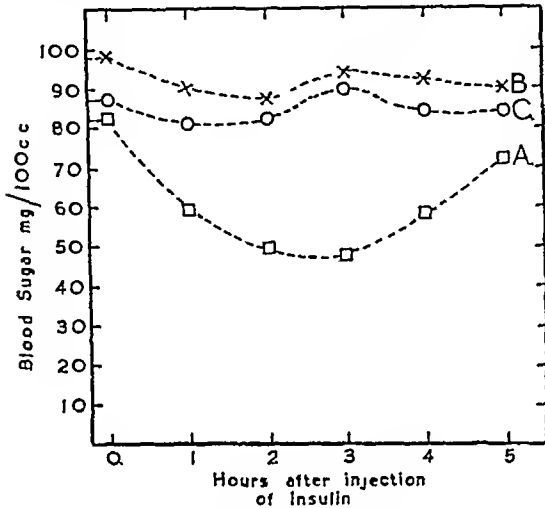


FIGURE 1 Hypoglycemic Action of Five Units of Subcutaneously Administered Insulin in Dogs Fasting Eighteen Hours

Curve A normal dog Curve B dog which had become refractory to the diabetogenic action of an anterior pituitary extract, after an initial response Curve C dog which had not yet become diabetic as the result of treatment with anterior pituitary extract

secretions of the pars intermedia may be of significance in this connection, most of the results to be discussed in the present communication have been obtained with extracts of the anterior lobe. It must be admitted, however, that these extracts were contaminated with traces of the melanophore expanding principle from the pars intermedia

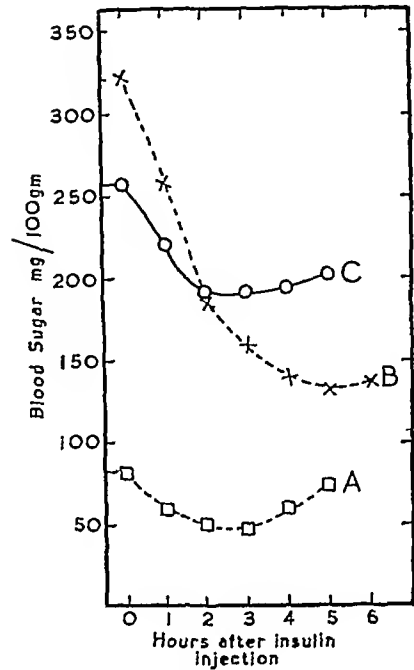


FIGURE 2 Hypoglycemic Action of Five Units of Subcutaneously Administered Insulin in Dogs Fasting Eighteen Hours

Curve A normal dog Curve B dog made permanently diabetic by treatment with anterior pituitary extract response determined some months after the cessation of injections Curve C dog made temporarily diabetic by treatment with anterior pituitary extract response determined during the period of injections

The absolute fall of blood sugar in Curve C is greater than that in the control curve, but the percentage fall is much less. Curve C therefore illustrates diminished sensitivity to the action of insulin. In Curve B both the absolute and the percentage fall of blood sugar level are greater than the corresponding values for the control curve. Curve B therefore illustrates no diminished sensitivity to the hypoglycemic action of this dose of injected insulin

PLATE 1 (Histological preparations by Mr K C Richardson)

A An islet of Langerhans from the pancreas of a dog which had become refractory to the diabetogenic action of an anterior lobe extract showing a mitotic figure in a beta cell. The beta cells are partly degranulated the alpha cells are normal. Magnification, $\times 710$

B An islet of Langerhans from the pancreas of a dog made temporarily diabetic by anterior lobe extract, showing advanced stages of hydropic degeneration in four islet cells. (The section has not been stained specifically to demonstrate the cell-types.) Magnification, $\times 580$

C An islet from the pancreas of permanently-diabetic Dog 44 consisting mainly of alpha cells with a few partly degranulated beta cells. The specimen was taken twelve months after the cessation of injections. Magnification, $\times 610$

D An islet from permanently diabetic Dog 44. In the islet the beta cells are agranular and presumably in a state of exhaustion. The alpha cells have become densely crowded together. The print has been overexposed to emphasize the agranular condition of the beta cells. Magnification $\times 470$

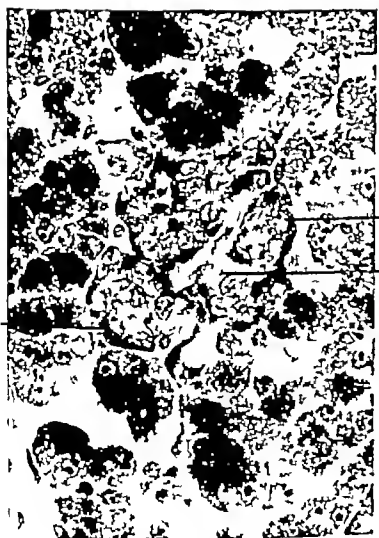
KEY a alpha cell b beta cell db beta cell depleted of its specific-staining cytoplasmic granules pb beta cell which has lost part of its cytoplasmic granules h cell undergoing hydropic changes m mitotic figure



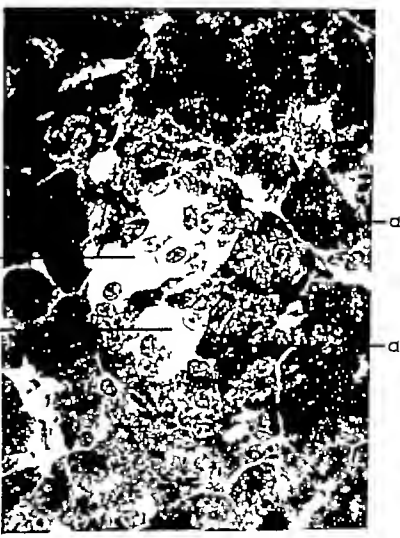
A



B



C



D

sequently exhibit insensitivity to the hypoglycemic action of a test dose of insulin, injected at the end of a short period of fasting, even though the blood sugar level is not significantly raised by the treatment with pituitary extract (Fig 1). If, however, daily injections of a crude extract are continued for some days, a high fasting blood-sugar level may be found, still associated with insulin insensitivity (Fig 2) (cf di Benedetto), which, however, is more marked in the rabbit than in the dog. There is good evidence that the anterior pituitary principle causing the rise of blood-sugar level (the diabetogenic principle) is not identical with that inducing insensitivity to the hypoglycemic action of insulin (the glycotropic principle [Young, 1936, 1938 a]).

When a dog receives daily injections of a crude anterior pituitary extract for some days, after the latent period during which the general blood-sugar level is not significantly raised although insensitivity to injected insulin develops, the blood-sugar level slowly rises and the symptoms of diabetes appear, that is, the animal exhibits hyperglycemia, glycosuria, polyuria, ketonuria, hyperlipemia and acidosis, the sugar tolerance is diminished and the administration of glucose is followed by a subnormal rise of the respiratory quotient, much of the ingested sugar being excreted in the urine. The main differences between the diabetic condition produced by treatment with anterior pituitary extract and that following removal of the pancreas are (in dogs) the relative insensitivity to the hypoglycemic action of insulin, the tendency to gain rather than lose weight and the high liver-glycogen content of the animals made diabetic by pituitary extract (confirmed in our laboratory see also Young, 1937 b, and Marks and Young, 1938 a).

Houssay observed that the diabetic condition induced by treatment with anterior pituitary extract was greatly diminished in intensity, or entirely abolished, by fasting, and that the condition disappeared within a few days of the cessation of daily injections of extract. E. I. Evans, and later Young (1936), found that the symptoms of diabetes in the dog disappeared during the course of seven to ten days, in spite of daily treatment with the same dose of extract. Young further observed that the symptoms of diabetes reappeared if the amount of extract injected daily was suitably increased but again subsided despite the continuation of daily treatment with the increased amount of extract. A further rise in the amount of extract injected daily again resulted in a reappearance of the diabetic condition, which,

as before, disappeared when the same amount of extract was administered each day for some days. It was found that this disappearance of the symptoms, followed by their reappearance with an increase in the amount of extract injected daily, could occur a number of times, it was observed in rabbits, cats and dogs, although the last-named species appeared to be the most generally satisfactory for investigations of this nature. We have observed that those animals which have become resistant to the diabetogenic action of the extract are nevertheless still relatively insensitive to the hypoglycemic action of injected insulin (Fig 1), and that the fasting liver glycogen content is still abnormally great (cf Young, 1937 b). For instance, Dog 72, which had become refractory to the diabetogenic action of an anterior lobe extract, but which, nevertheless, was still relatively insensitive to the hypoglycemic action of 5 units of insulin, possessed 99 per cent of liver glycogen and 2.25 per cent of muscle glycogen after a fast of twenty-four hours. These experiments indicate that development of refractoriness to the action of the diabetogenic principle in the pituitary extract is not necessarily accompanied by the development of resistance to its glycotropic (anti-insulin) action, nor to its action on the retention of glycogen during a short fast.

THE "PANCREATROPIC" ACTION OF ANTERIOR PITUITARY EXTRACTS

Examination of the islets of Langerhans of dogs which had developed refractoriness to the diabetogenic action of an anterior pituitary extract revealed unusual mitotic activity (Plate 1 A; Richardson and Young, 1938) associated with hydropic degeneration (Plate 1 B, cf Allen, 1922). Sometimes these two processes were found to be proceeding simultaneously in the same islet. It should be stressed that mitoses in islet cells in the pancreas of a normal dog are so rare as almost entirely to escape observation. The unusual mitotic activity in the islets suggested the possibility that the animals had become resistant to the diabetogenic action of the extract because the islets had hypertrophied and were secreting more insulin. It was, of course, possible that the mitotic activity represented nothing more than replacement of cells which had undergone hydropic degeneration. Nevertheless, we were particularly interested in the statement by Anselmino, Herold and Hoffmann that anterior pituitary extracts possess a "pancreatropic" action. According to these workers the administration of an anterior pituitary extract to normal rats results

in a few days in a substantial increase in the number and size of the islets of Langerhans of the pancreas. They ascribe this increase to the action of a "pancreatotropic substance" believed to be present in the pituitary gland. This substance was found to cause not only hyperplasia of the islets but also an increase in the amount of insulin secreted by the islets, as shown by the fall of blood sugar occurring immediately after injection of an extract (Anselmino and Hoffmann). In the experiments of Anselmino and his colleagues the increase in the size and number of the islets was assessed solely on the basis of the histological appearance of sample sections of the pancreatic tissue from pituitary-treated animals, a method which is obviously open to objection. It is therefore not surprising that there has been much disagreement with respect to the question of this alleged pancreatropic action of pituitary extracts (for references see Richardson and Young 1937). Richardson and Young (1937), using a tedious but objective method for the quantitative determination of the pancreatic islet tissue in the rat found that the amount of islet tissue in the animals which had received daily injections of a crude pituitary extract for some weeks was about double that in control animals. They were, however, unable to confirm the activity of the type of extract used by Anselmino et al. under the conditions defined by the latter workers. More recently Marks and Young (1939) have found that the insulin content of the pancreas of the pituitary-treated rat may be more than twice that of control animals, suggesting that the extra islet tissue formed as the result of the hypophyseal stimulus, is functionally active.

The physiological significance of this pancreatropic action of pituitary extracts is difficult to determine in the light of experiments by Krischesky and by Adams and Ward, demonstrating that removal of the pituitary gland may be followed by an increase in the amount of pancreatic islet tissue. Moreover Krischesky using a quantitative method for the assessment of islet tissue, found that treatment of hypophysectomized rats with crude anterior lobe extract depressed the rise in the amount of islet tissue in the pancreas which occurred in hypophysectomized animals in the absence of such treatment. Nevertheless, it seems proved that the treatment of normal rats with anterior pituitary extracts can increase both the amount of islet tissue and the amount of insulin found in the pancreas and this effect will be described as a pancreatropic effect of the pituitary extracts. In the absence of a demonstration of an appropriate insufficiency syndrome, it is clearly unwise to speak of a pancreatropic hormone.

As the type of pituitary extract which was effective in increasing the amount of islet tissue and of insulin in the pancreas of the rat was also active in producing the symptoms of diabetes in dogs, it seemed possible that the islet hypertrophy was a compensatory response to the diabetic condition induced by treatment with the extract, prompt and more effective in the rat than in the dog. However, the blood sugar levels of rats receiving daily injections of these crude extracts were within normal limits (Richardson and Young 1937, Young 1938a), and although the possibility could not be entirely ruled out it seemed improbable that the islet hypertrophy could be merely a compensatory response to the diabetogenic action of the extract.

Some noteworthy experiments by Houssay and Foglia (1936) involving the grafting of the pancreas from one dog into the neck of another have demonstrated that the pancreas of a dog which is temporarily diabetic as the result of treatment with anterior pituitary extract is secreting less insulin than the pancreas of the normal dog. This decreased insulin secretion may result from a partial exhaustion of the power of the islets to secrete insulin brought about by the raised blood sugar level or it may be due to a direct action of the pituitary extract on the islets depressing the secretion of insulin. Whatever may be the explanation of these results, it seems reasonable to suppose that the dog is able to develop refractoriness to the diabetogenic action of a small daily dose of anterior pituitary extract, because the pancreatropic action of the extract has made more insulin available.

THE PRODUCTION OF A PERMANENTLY DIABETIC CONDITION IN THE DOG BY TREATMENT WITH ANTERIOR PITUITARY EXTRACT

As the dog was found to be capable of developing refractoriness to the diabetogenic action of the daily administration of a relatively small dose of anterior pituitary extract it was of interest to determine whether or not such refractoriness would develop when a very large dose was injected daily for some days. With this object in view Young (1937a, 1938b) gradually increased the amount of extract administered daily to a dog in such a way that the amount eventually administered each day was equivalent to 25 gm of fresh ox anterior lobe and found that refractoriness to the daily administration of this amount of extract was not developed. Moreover, when the daily injections of extract were stopped the diabetic condition continued and had apparently become permanent (Young 1937a). Later it was found that if the amount of extract administered

daily to the dog was increased after each three-day period, the development of the refractory condition could be avoided (Fig 3), and a permanently diabetic condition thus induced more rapidly. One dog was made permanently diabetic in this manner after only eleven days' treatment with pituitary extract. Campbell and Best, Houssay, Biasotti and Dambrosi, and Dohan and Lukens have recently confirmed this observa-

glycosuria is almost completely suppressed for a long period. On the contrary, the diabetic condition tends to increase rather than to decrease in severity with the passage of time. It is convenient to consider the response of the dog to the daily administration of diabetogenic pituitary extract as divisible into a number of phases. First, the latent period, during which hyperglycemia and glycosuria are not observed, although a relative insen-

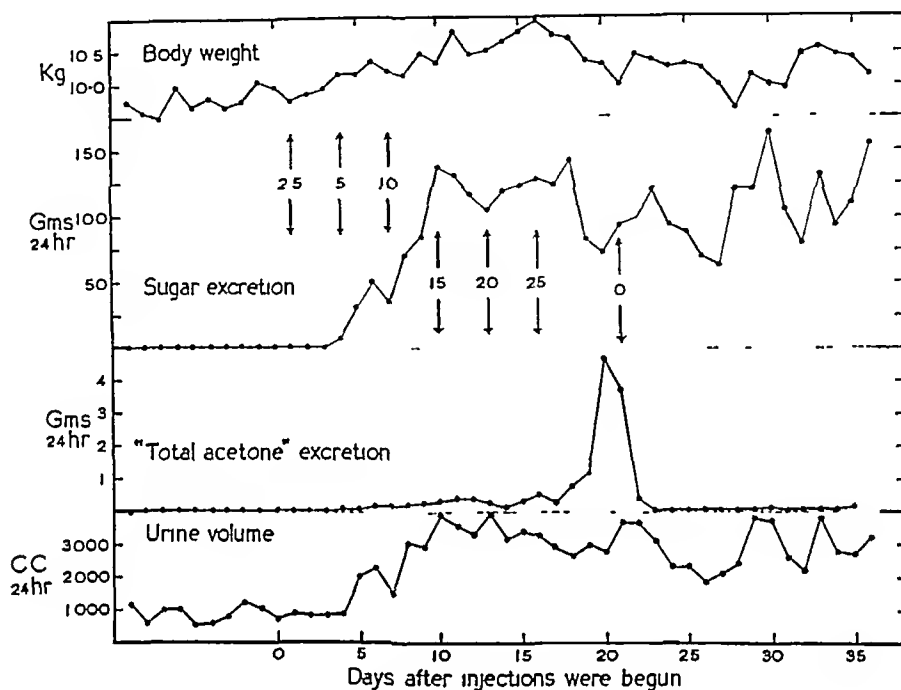


FIGURE 3 Data Relating to Dog 44 during the Period of Establishment of the Permanent Diabetes

The figures on the arrows give the weight in grams of fresh ox anterior pituitary tissue used to prepare the amount of crude extract injected daily, from the day indicated by the arrow, onward. The injections ceased on the day indicated by the arrow marked "0". The ketonuria fell to a low level following the cessation of injections but rose later. (Reproduced from Proc. Roy. Soc. Med. 31:1305-1316, 1938, by permission of The Royal Society of Medicine.)

tion, that is, that a clearly defined and permanent diabetic condition may be produced in dogs by a short period of treatment with crude anterior pituitary extract.

In our experience a period of intense treatment is required to bring about the permanently diabetic state, and if treatment is stopped before a sufficient intensity has been reached and maintained for some days, the diabetic condition may disappear after the daily injections of pituitary extract cease. We have gained the impression that there is a definite point at which the phase of temporary diabetes resolves into a condition of permanent diabetes. According to our experience, once the permanent state has been produced it shows no sign whatever of remission, even though, as the result of treatment with insulin,

sensitivity to the hypoglycemic action of injected insulin is found. Second, the phase of temporary diabetes, during which there is still a relative insensitivity to the action of administered insulin, and the liver-glycogen level is high. Third, the refractory phase, during which the blood-sugar level is normal but insulin insensitivity persists, and a high fasting liver-glycogen level is found. The development of this refractory phase can be circumvented by rapidly increasing the amount of extract injected daily. Finally, if the amount of extract administered each day is increased to a sufficient degree, the resurgent phase of temporary diabetes may resolve into a permanently diabetic condition, which persists indefinitely after cessation of treatment with pituitary extract. When the response to insulin, of dogs thus made per-

manently diabetic, is determined some time after the injections of extract have ceased, it is found to indicate no obvious insulin insensitivity of the type found during the phase of temporary diabetes (Fig 2), while treatment with pituitary extract is still proceeding.

There are a number of points about the transition from the temporary to the permanent condition of diabetes which may be mentioned. A symptom which we have found of use, in indicating that the permanent condition is nascent, is a rapid and substantial increase in the ketonuria (cf Fig 3). The excretion of ketone bodies may be only slight during the temporary phase, even though the glycosuria is intense nevertheless, with dogs on a liberal mixed diet such as we have used, the ketonuria may suddenly increase at the time

later increases, and in some of our animals we have observed a progressive increase in ketonuria over a period of a year or more. In the absence of treatment with insulin the body weight may fall slightly or remain steady for a time despite the substantial glycosuria provided the dog is given enough protein food to cover the calories lost by the excretion of combustible material in the urine. The appetite of the animals is, of course, very large.

THE METABOLISM OF DOGS MADE PERMANENTLY DIABETIC BY TREATMENT WITH ANTERIOR PITUITARY EXTRACT

An investigation of the metabolism of dogs made permanently diabetic by treatment with anterior pituitary extract undertaken in collabora-

TABLE 1 *Insulin Requirements of Pituitary-Diabetic Dogs and of Depancreatized Dogs**

TYPE	DOG NO.	INSULIN GIVEN	GLUCOSE EXCRETION	NITROGEN EXCRETION	UNSELECTED GLUCOSE EXCRETION (N=19.1)	GLUCOSE RETAINED PER UNIT OF INSULIN	INITIAL BODY WEIGHT	BODY WEIGHT CHANGE
		<i>units per day</i>	<i>gm. per day</i>	<i>gm. per day</i>	<i>gm. per day</i>	<i>gm.</i>	<i>kg.</i>	<i>kg. per day</i>
Pituitary-diabetic dog.	44	60	11.0	19.4	9.9	1.9	10.8	+0.01
		50	23.7	18.7	25.1	2.0	8.9	+0.06
		20	91.8	20.8	85.7	1.9	9.8	—
	50	40	5.4	18.5	7.6	2.9	8.1	+0.04
		25	21.1	18.1	24.7	3.9	7.5	+0.06
Depancreatized dog	60	20	4.2	19.8	1.7	6.1	10.9	+0.02
	67	25	9.9	18.7	11.3	4.3	6.7	+0.03
	69	25	10.0	19.3	9.3	4.6	7.8	+0.02
	70	30	8.4	17.8	13.1	3.7	8.3	+0.01
	71	30	10.4	17.5	16.2	3.6	9.6	+0.02
Depancreatized pituitary-diabetic dog	44	30†	38.7	19.2	38.3	2.0	10.5	+0.05

The diet consisted of 500 gm. of raw meat, 250 gm. of raw pancreas and 50 gm. of glucose daily; the figures are mean daily values for periods sensitive periods of 1 or 2 weeks.

*No glycosuria with 50 ius of insulin per day

at which we believe that the temporary evolves into the permanent diabetes, two of our dogs lapsed into what appeared to be diabetic coma at this point. The body weight tends to increase during the period of injections, but just before the condition of permanent diabetes has apparently been established, the body weight sometimes declines to its initial value, or a little below. It appears improbable that the increase in weight during the period of injections is due entirely to growth, although some true growth probably occurs. The increase is of such magnitude in some cases as to render improbable the idea that it is due entirely to water retention but this possibility cannot be entirely ruled out. Deposition of fat might in part account for such a rapid increase.

When the daily injections of pituitary extract are stopped after the permanent diabetes has been established, the ketonuria may fall to a very low level, although the glycosuria continues unabated or increases in intensity. The ketonuria

with my colleague, Mr H P Marks, has revealed some interesting differences between the diabetic condition of these animals and that which follows pancreatectomy in the dog (Young, 1938b). In particular, the amount of insulin required to regulate the glycosuria of the pituitary diabetic dog appears to be significantly greater than that required for the depancreatized dog consuming and absorbing the same amount of food (Table 1).

In order to enable a careful comparison to be made between the characteristics of the pituitary diabetic dog which has its digestive system intact and those of the depancreatized dog which lacks pancreatic enzymes, we fed dogs of both types on a diet containing a large amount of raw pancreas, our diet being based on that used for depancreatized dogs by Dr C. H. Best and his colleagues at the University of Toronto. With this diet it was possible to rectify almost completely the deficient intestinal absorption of the depancreatized dog and to avoid the complica-

tion of fatty livers due to a deficiency of choline or other substances. Determinations of urinary and fecal nitrogen contents of depancreatized dogs receiving this diet indicated that more than 90 per cent of the protein was absorbed from the bowel. In many experiments the depancreatized dogs were given slightly more food than the pituitary diabetic dogs, in order to be certain that they were absorbing an equivalent amount of protein.

The results given in Table 1 show that the insulin required to control the glycosuria of pituitary diabetic Dog 44 was nearly twice that required by any of the depancreatized dogs examined. On the other hand, pituitary-diabetic Dog 50 appeared to require no more insulin than did

quirement is generally confirmed it may be that the acinar tissue of the pancreas plays a hitherto unsuspected role in carbohydrate metabolism. Campbell and Best have observed in two dogs made permanently diabetic by treatment with anterior pituitary extract, little aggravation of the diabetic state resulted from removal of the pancreas. However, before pancreatectomy these pituitary-diabetic dogs did require more insulin to control their glycosuria than did ordinary depancreatized dogs, and fortunately the result of depancreatizing a pituitary diabetic dog, which was more resistant to insulin than any completely depancreatized dog they had ever observed, was not deterred. In spite of the large amount of insulin

TABLE 2 Data Obtained in Dogs Receiving a Meat Diet with No Insulin*

TYPE	DOG NO.	URINE VOLUME cc. per day	GLUCOSE EXCRETION gm. per day	NITROGEN EXCRETION gm. per day	D/N RATIO (CORRECTED)	KETONE EXCRETION gm. per day	INITIAL BODY WT. kg.	BODY WT. CHANGE kg. per day
Pituitary diabetic dog	28	1550	94.8	25.7	3.40	0.70	10.2	0
	40	1450	89.2	26.9	3.09	0.28	8.3	0
	44	2950	95.5	27.6	4.00	5.01	8.8	0
	50	1600	91.0	25.0	3.45	1.80	8.2	0
	51	2750	102.9	26.6	3.69	4.03	7.2	0
Depancreatized dog	60	2000	91.2	23.7	3.47	2.96	8.9	-0.07

*The figures are mean daily values for 1 or 2 weeks.

depancreatized male dogs. It should be mentioned that Dog 50 appeared, as judged by other criteria, to be somewhat less intensely diabetic than most others in our group of dogs made permanently diabetic by pituitary extracts. Although the insulin requirement of other dogs fed on the meat plus glucose diet was not accurately determined, much evidence has accumulated to show that the insulin requirement of at least two other dogs was similar to that of Dog 44, and appeared therefore to be significantly greater than that of the depancreatized dog. It is clear from these results that the severity of the permanently diabetic condition produced by treatment with anterior pituitary extract may vary substantially from dog to dog.

The results of Allan indicate that when a depancreatized dog is given different amounts of insulin while receiving the same amount of food each day, a plot of the logarithm of the number of grams of glucose retained each day, against the logarithm of the insulin dosage, should give a straight line. We have been able to confirm this both for depancreatized dogs and for our pituitary-diabetic dogs.

When Dog 44 was depancreatized, the amount of insulin required to control the glycosuria was slightly and possibly significantly diminished (Table 1). If such a diminution in insulin re-

quired to control the glycosuria of the pituitary diabetic dogs, they are able to survive long periods without treatment with insulin, provided they are supplied with sufficient food. This is illustrated in Table 2, in which is included for comparison figures relating to a depancreatized dog which lost least weight on a meat (raw plus raw meat) diet. In our experience the depancreatized dog usually loses body weight more rapidly than did Dog 60 during the period illustrated. It is interesting to note that the ratio (corrected for the presence of small amounts of preformed carbohydrate in the meat) of ketone excretion of Dogs 44 and 51 are both significantly higher than the corresponding figures for the depancreatized dog, yet the pituitary dogs were able to maintain body weight under these conditions, whereas the depancreatized dog was not able to do so.

The difference in ability to survive without insulin therapy is well illustrated in Figure 1, which are illustrated data relating to a period during which pituitary-diabetic Dog 44 and depancreatized Dog 60 were both gradually deprived of insulin under similar conditions. The result of insulin deprivation in Dog 60 was a rapid loss of body weight and death, although Dog 44, after an initial loss of body weight, continued to live in good condition without insulin for

months. This was in spite of the fact that, under similar conditions, Dog 44 required about three times as much insulin as did Dog 60 in order to regulate the glycosuria. It should be emphasized, however, that if the pituitary-diabetic dogs are suddenly deprived of insulin after a period of

values for the other dogs lying between 3.4 and 40.1. The ketone excretion appeared to vary with the type of meat consumed (*vide infra*). As the result of a short fast the D/N ratio fell to a figure close to the classical value found by Minkowski, namely 2.8.1. At the end of

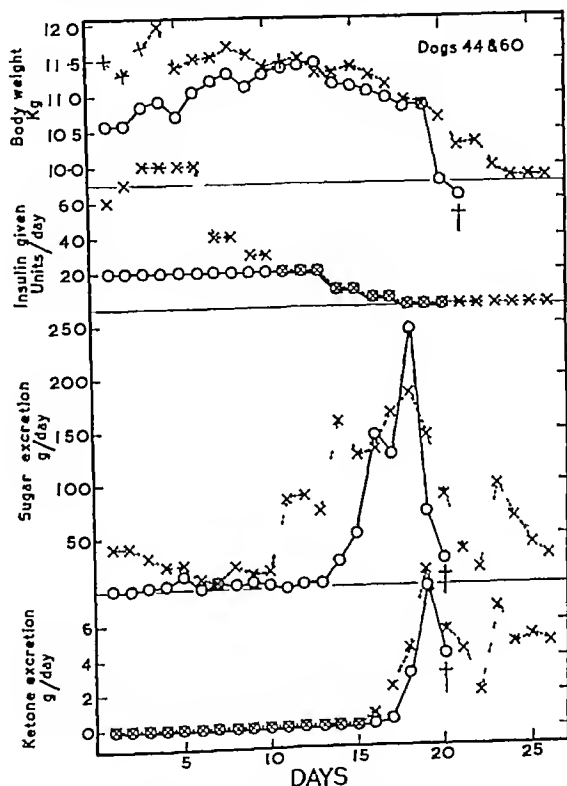


FIGURE 4 Data Relating to Pituitary Diabetic Dog 44 (dashed curves) and to Depancreatized Dog 60 (continuous curves) at a Time When Insulin Was Gradually Withdrawn after a Period of Experimental Therapy

Both dogs were receiving and absorbing the same amount of food during the period of insulin administration. Dog 60 died on the twentieth day of the period illustrated.

therapy, they may lapse into a coma which terminates fatally (cf Young 1937 a).

In our experience the corrected D/N ratios and ketone excretions of the pituitary-diabetic dogs vary substantially from time to time, but only with Dog 40 did the corrected D/N ratio on a meat diet fall even slightly below 30.1 the

a forty-eight hour fast the blood sugar level of our dogs averaged 250 mg per 100 cc.

When 50 gm of glucose was added to the food of our pituitary-diabetic dogs receiving a meat diet, nearly the whole of the extra glucose was excreted in the urine, as indicated by the relative constancy of the corrected D/N ratios. All

though the values varied from time to time, on the average about 90 per cent of the added glucose was found in the urine. When 50 gm of glucose was given by mouth to a fasting pituitary-diabetic dog, the sugar-tolerance curve was of a strongly diabetic type (Fig 5). Respiratory data obtained

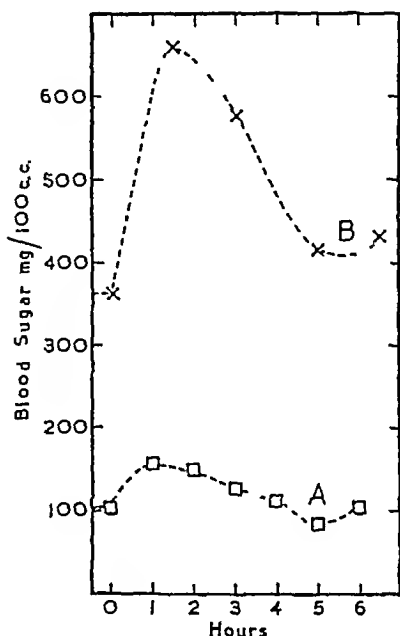


FIGURE 5 Sugar Tolerance Curves in Dogs

Curve A average blood-sugar response of 5 normal dogs to the oral administration of 50 gm of glucose
Curve B average response of 4 pituitary-diabetic dogs to the oral administration of 50 gm of glucose

by Mr Marks showed that no significant rise of the respiratory quotient occurred as the result of the administration of 50 gm of glucose to these dogs.

When the pituitary-diabetic dogs received a high-carbohydrate (biscuit) diet, the glycosuria was intense, although the ketonuria was less than when the animals were receiving a protein diet. On the average all the preformed carbohydrate in the diet was excreted in the urine, but when the total available carbohydrate in the diet was calculated (assuming that protein in the food was converted to sugar according to a D/N ratio of 3.6/1) it was found that only about 85 per cent of all the available carbohydrate appeared in the urine. It is therefore to be assumed that the pituitary-diabetic dogs are able to oxidize a small amount of sugar when the diet contains a high proportion of this material.

Some of our pituitary dogs tolerated a high-fat diet, consisting of beef suet only. On such a diet, glycosuria and ketonuria were both diminished (Marks and Young, 1938b, Young, 1938c), and in the case of one dog which tol-

erated the diet for some weeks, it was possible to demonstrate a substantial increase in sugar tolerance as the result of feeding this fat diet. The addition to the fat of raw meat, but not of cooked meat or casein, resulted in an increase in ketonuria (Young, 1938c). It is difficult to reconcile these results with the classic theories regarding ketone formation from fatty acids, for it appears from our experiments that the excretion of ketone bodies by the pituitary-diabetic dog is conditioned, not by the amount of fat in the diet, but by the amount of raw meat or some extractable substance present in the raw meat.

Himsworth has divided human diabetic patients into two classes, those who are insulin-sensitive and those who are insulin-insensitive. These two classes are differentiated on the basis of the form of the sugar-tolerance curve obtained when a small dose of insulin is given subcutaneously at the same time as the patient takes a test dose of glucose by mouth. As judged by the results of a similar test carried out on Dog 44 our pituitary-diabetic dogs fall into the insulin-sensitive class.

De Wesselow and Griffiths found that the plasma from a certain type of diabetic patient resembles an extract of the anterior pituitary gland in that the administration of such plasma to a fasting rabbit results in a depression of the animal's sensitivity to the hypoglycemic action of administered insulin. We have not been able to obtain similar results with plasma from our pituitary-diabetic dogs.

THE ISLETS OF LANGERHANS OF THE PANCREAS IN PITUITARY-DIABETIC DOGS

The general sensitivity to insulin of the pituitary-diabetic dogs did not suggest that the diabetic condition of these animals persists because of continuous hypersecretory activity on the part of the anterior pituitary gland. In the circumstances it was of interest to examine the histological appearance of the endocrine glands of these animals, and in particular the islets of Langerhans of the pancreas. A careful histological examination was carried out by my colleague, Mr K. C. Richardson (Richardson and Young, 1938), who could find no obvious changes in the thyroid, adrenal or pituitary glands of these animals. The pancreatic islets, however, showed changes which ranged from depletion of the cytoplasmic granules of the beta cells to complete replacement of islets by hyaline material. In some cases (Plate I C and D) the beta cells were greatly diminished in number and many islets consisted either of clumps of alpha cells only, or of alpha cells together with hyaline material. The pancreas of Dog 40 was of particular interest, as the only obvious change was a diminution

in the cytoplasmic granule content of many of the beta cells, although some islets contained beta cells with a normal content of chromophil granules. It should be emphasized that hydropic degeneration was not an obvious feature of the pancreatic islets of these permanently diabetic dogs although, as has been mentioned already, degeneration of this type was common in the islets of dogs which were actually undergoing treatment with diabetogenic pituitary extracts. It seems possible that obvious hydropic degeneration is brought about by the strain of a sudden induction of a diabetic condition, but that, when a permanent diabetes has been established, the adjustment is such that any degeneration of the hydropic type is going on at a rate so slow as not to be obvious. Beta cells in hydropic degeneration were observed in a few islets of Dog 40 but not in any of the islets of other permanently diabetic dogs in which a careful examination was made, the paucity of beta cells in these cases may, of course, have been caused by previous hydropic changes.

Mr Richardson reports that a constant finding in the pancreatic tissue of dogs which have been treated with anterior pituitary extracts is vacuolation of the intralobular duct epithelium. This change has been observed in pancreatic tissue from dogs which have been treated with anterior lobe extracts having no evident diabetogenic activity. If new islet cells proliferate from the epithelium of the intralobular ducts during life, as they undoubtedly do in the embryo, the observed changes in the duct epithelium may be of significance in the search for a reason to account for the lack of replacement of the degenerated islet tissue in these permanently diabetic dogs.

We have now to consider whether, in every case, the changes in the islets of Langerhans observed in our dogs are sufficient to account for their permanently diabetic condition. In most of our animals the islets were so abnormal that there is little difficulty in assigning to this change alone the persistence of the diabetic condition. In the case of Dog 40, however, the changes in the islets were of such a slender nature as to render doubtful the assumption that they alone were able to account for the permanently diabetic condition of this animal. It is true that the condition was somewhat less intense than that of the other dogs we have examined but corrected D N ratios of about 30:1 were observed when this dog was receiving a full-protein diet, and there is no reason to doubt that it was suffering from a severe permanent diabetes. Also, in the case of Dog 44 the changes in the islets are relatively slight, when the intensity of the diabetic condition of this dog is taken into account. It is therefore unwise to

consider as precluded the possibility that the diabetic condition of some or all our dogs results, in some measure, from extrapancreatic factors. There is no evidence, as we have seen, that overactivity of the anterior pituitary lobe is of importance in this connection but the possibility of there being a deficiency of precursors of insulin might conceivably be of importance. It should be mentioned however, that belief in the sufficiency of the changes in the pancreatic islets to account for the persistence of the diabetic condition is not rendered impossible by the observation that the pituitary-diabetic dogs may require more insulin for the regulation of glycosuria than do depancreatized dogs. As has already been pointed out this difference in insulin requirement may be due to the presence of the pancreatic acinar tissue in the pituitary-diabetic dogs.

THE SIGNIFICANCE OF THE ANTERIOR PITUITARY GLAND IN HUMAN DIABETES

As the result of Houssay's fundamental observations the existence of a definite type of diabetes induced by overactivity of the anterior pituitary gland was recognized. This condition could be most easily differentiated from diabetes resulting from a simple deficiency of insulin by the relative insensitivity to the hypoglycemic action of injected insulin exhibited by cases of the former type (cf di Benedetto). Thus a convincing explanation was forthcoming for the existence of those interesting cases of human diabetes mellitus in which an extreme insensitivity to the hypoglycemic action of insulin is found, in some cases of this type many hundreds or even thousands of units of insulin are required each day in order to control glycosuria although it seems improbable that so much insulin is secreted by the normal human pancreas. Only a very small number of human diabetic patients fall into such an insulin-resistant class however and in the remainder of the cases the condition is presumably to be ascribed to deficiency of function in the pancreatic islets. It is to be inferred from Houssay's results that in all cases of diabetes the severity of the condition is determined by the activity of the anterior pituitary lobe, but, in the absence of demonstrable insulin-resistance or of gross insensitivity to the action of insulin it is to be presumed that the pituitary gland is secreting no more than the normal amount of diabetogenic principle. In such cases the existence of the condition is presumed to be due primarily to dysfunction of the islets of Langerhans of the pancreas. It is true that in many cases of human diabetes no clearly defined lesions have been ob-

served in the pancreatic islets (Warren), and the changes in the islets of our pituitary-diabetic Dog 40 were so slight as to have easily escaped detection, had not the tissue been fixed immediately after removal from the animal. Clearly, the possibility that an extrapancreatic factor is involved in the maintenance of the diabetic condition in such a case must be borne in mind.

Is it possible that a case of human diabetes resulting from lesions of the pancreatic islets may be primarily of pituitary origin? We have seen how in dogs a short period of intense treatment with anterior pituitary substances can result in damage to the islets of Langerhans and the establishment of a permanently diabetic state. In these dogs there is no obvious persistent effect of the short period of treatment with pituitary extract, other than the islet lesions and the diabetic condition, although the thyroid glands are greatly stimulated as the result of the treatment with a relatively crude anterior pituitary extract, they return to a normal condition after the cessation of treatment, and, in dogs which were examined a year or so after the permanent diabetes had been established, normal thyroid glands were found. If the results of these experiments may be used for an analysis of the etiology of human diabetes, it seems possible that cases of diabetes mellitus in which no obvious indications of pituitary hyperactivity exist, and in which lesions of the islets of Langerhans of the pancreas are presumed to be the primary cause of the condition, may nevertheless have originated as the result of a short period of overactivity of the anterior pituitary gland. It is becoming clear, as the result of investigations on the action of the sex hormones, that the secretory activity of the anterior pituitary gland may vary substantially from time to time. It is conceivable that a short period of hyperactivity might result in the liberation of such excessive amounts of diabetogenic principle as to induce those irreversible changes in the islets of Langerhans which result in the establishment of a permanently diabetic condition. If this is so, then we may have to seek the primary cause of many cases of human diabetes in the anterior lobe of the pituitary gland, rather than in the islets of Langerhans of the pancreas, although defective insulin production by the pancreatic islets may be the secondary and direct cause of the condition.

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GAS-BACILLUS INFECTION OF THE ABDOMINAL WALL

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IT IS our desire in this paper to report and discuss two cases of gas-bacillus infection that followed the operation of cecostomy for cancer of the large bowel. Few if any complications of abdominal surgery are more serious in their possibilities than gas-bacillus infections of the abdominal wall. This fact and also the rarity of the condition warrant our presenting these cases considering the literature on the subject and discussing the treatment that gave recovery to both our patients.

Those of us who had experience with the surgery of wounds in the World War recall too vividly not only the frequency of gas-bacillus infection but also its tremendous mortality. Millar¹ for example, reported 1529 cases of gas gangrene among 25,272 surgical cases in the American Expeditionary Forces.

In civil surgery gas gangrene is seen most commonly in crushing injuries of the extremities with or without fractures. Nevertheless, *Clostridium welchii* infection has occasionally followed nearly every type of ordinary surgical operation. Cases have been reported following appendectomy, herniectomy, colostomy, ileostomy and cholecystectomy. One of us (H. M. C.) has seen it follow a traumatic rupture of the liver.

The occurrence of *Cl. welchii* infection as a complication of cecostomy, enterostomy or colostomy with which we are more particularly concerned, has been previously observed and reported by a number of authors. Butler² reports a fatal case occurring sixty-seven hours after a Witzel cecostomy for intestinal obstruction due to volvulus of the cecum. In the same paper he records a second case following operation for gangrenous appendicitis with abscess.

Butler and Rhoades³ report 2 cases following enterostomy for small-bowel obstruction in a series of 180 cases. The first occurred forty-eight hours after enterostomy, and the patient recovered after opening of the wound and institution of serum therapy. The second case developed within twenty-four hours after enterostomy for a strangulated ventral hernia. This case terminated fatally on the eighth postoperative day.

Eckhoff⁴ reports a case of subacute intestinal obstruction in a man of fifty-nine of seven days

duration for which ileostomy was done. The patient died twenty-four hours after operation with extensive gas-bacillus infection of the abdominal wall. Swabs yielded *Cl. welchii* in pure culture. A second case is reported in a woman of sixty-two with intestinal obstruction due to carcinoma of the colon. Colostomy was done and on the fifth postoperative day emphysema of the abdominal wall developed, the following day she expired. Serum was not given.

Orr⁵ reports 3 fatal cases following Witzel ileostomy. The first developed on the fifth postoperative day in a case of appendiceal abscess; the second occurred on the second postoperative day in a case of strangulated hernia; and the third occurred on the seventh postoperative day for intestinal obstruction of undiscovered origin.

ETIOLOGY

Clostridium welchii (*Bacillus welchii*, *B. aerogenes capsulatus* or *B. perfringens*²⁰) as well as other anaerobes (*Cl. oedematis maligni* or *Vibrio septique*, *B. histolyticus* and others) are widely scattered in garden soil and earth in general. They are, in fact, ubiquitous in their distribution. Gay¹² states that Bull obtained his most toxic strain of *Cl. welchii* from the lining of an old overcoat and Gage¹¹ has observed gas bacilli in wool and is of the opinion that they are found especially in woolen goods. That they are normal inhabitants of the intestinal tract of both man and animals seems well established.

In 1893 Veillon and Zuber²¹ reported finding *Cl. welchii* (*B. perfringens*) in 98 per cent of 26 cases of appendicitis. Lanz and Tavel¹⁴ found *Cl. oedematis maligni* in 49 of 136 cases of appendicitis. Simonds²² reports finding *Cl. welchii* in 90 per cent of normal appendices removed at autopsy and in 100 per cent of cases if the appendix contained fecal matter. Jennings¹⁵ found that cultures from the contents of lumens of appendices removed at operation showed *Cl. welchii* in 90 per cent. In 1938 Bower et al.² found *Cl. welchii* in the flora of 60 per cent of 55 cases of gangrenous appendicitis associated with spreading peritonitis. Haerem et al.¹⁷ found *Cl. welchii* and *Escherichia coli* (*B. coli*) to be the predominating organisms recovered from the flora of closed intestinal loops in dogs.

It is generally agreed that in the absence of any pathologic disturbance of bowel function *Cl. welchii*

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clui as a normal inhabitant of the intestine is innocuous and produces no absorbable exotoxin. What, then, are the factors which bring about the manifestation of the potentially invasive and toxic properties of these organisms, and which give rise to clinical gas-bacillus infection of the abdominal wall, with its widespread destruction of tissue and profound toxemia, which in many cases is fatal?

Williams,³¹ in an excellent paper published in 1926, states that *Cl welchii* requires for the production of toxin a slightly alkaline or neutral medium, and that in an acid medium the toxin is destroyed. When the small bowel is obstructed conditions are excellent for the proliferation of the organism and production of its toxin. Obstruction to the large bowel likewise finally results in ideal conditions for the growth of the gas bacillus. Specimens of vomitus showed *Cl welchii* in eleven of twelve specimens taken by Williams from patients with acute intestinal obstruction, and in nineteen of twenty specimens from patients having general peritonitis. The intestinal contents in acute obstruction showed a high percentage of infection.

Given a medium suitable for the growth of *Cl welchii*, a second factor which increases the ease of growth of anaerobic organisms is the relative anoxemia and tissue anoxia which exist in a loop of obstructed intestine. Gatch¹² and others have clearly shown that gaseous distention of the bowel causes a decrease in blood flow through the bowel wall, which is in direct proportion to the elevation of the pressure, and that when the intraluminal pressure reaches the level of the diastolic pressure it ceases almost entirely. With the stage thus set, and with a cuff of gangrenous or ischemic bowel wall turned in around the enterostomy tube, and with muscle near by which has been more or less traumatized in opening the abdomen, it is perhaps surprising that this complication does not occur with great frequency when cecostomies are performed.

CASE 1. A B, a 67 year-old man was admitted to the hospital with a history of abdominal pain and obstipation of 9 days' duration. For 2 days prior to entry, crampy low abdominal pain had been severe and was accompanied by much rumbling and by vomiting.

Examination showed a soft, doughy distention of the abdomen, and a flat film revealed marked distention of the colon, particularly in the transverse and splenic portions. Barium enema revealed incomplete obstruction in the proximal sigmoid, suggesting torsion. The patient failed to show any sustained improvement during the period of preoperative preparation, and on the 4th day a cecostomy was done. A No. 18 catheter was inserted through a stab wound in the cecum without apparent soiling, and a cuff of bowel turned down around the tube by a double purse-string suture. Exploration at this time revealed a constricting annular carcinoma of the splenic flexure.

The patient's progress was entirely satisfactory until 6 p.m. on the first postoperative day, 29 hours after operation, when his temperature suddenly rose to 105.5°F, and his pulse to 140. He complained of abdominal discomfort, and was obviously confused and in a state of profound shock.

Examination of the wound showed a dull, coppery red discoloration of the skin about the incision and unmistakable crepitation on palpation. The peculiar so-called mousy odor commonly associated with this type of infection was apparent. A clinical diagnosis of gas-bacillus infection of the abdominal wall was made, which was subsequently corroborated by the laboratory study of cultures. The wound was opened and hydrogen peroxide dressings were begun and continued every 2 hours. The patient was immediately given 2 ampules (60 cc.) of polyvalent gas-bacillus antitoxin—the first intramuscularly and the second intravenously. In the next 24 hour period he was transfused, and 3 ampules of gas-bacillus antitoxin were given intravenously, in the 3rd 24 hour period 4 ampules were given, on the 4th day, 3 ampules, and on the morning of the 5th day, 1 ampule. For 3 days after onset the patient continued in a profound state of shock, and at intervals was delirious and disoriented. During this period there occurred a rapid spread of the fulminating local infectious process, with extension of the coppery discoloration and crepitation out into the right flank and across the midline covering an area fully 20 by 25 cm. In the region of the wound there was widespread destruction and sloughing of skin, muscle and fascia, accompanied by profuse drainage of a grayish-black watery discharge. At the end of the 3rd day after onset it was apparent that the process was receding, but antitoxin was continued for 2 more days. The wound slowly granulated in, and the patient's general condition gradually improved.

One month after the cecostomy was done the patient was again operated on through a left rectus incision. The descending and sigmoid portions of the colon below the annular lesion of the splenic flexure were greatly distended. The dilated loop passed through an arch-like congenital opening in the mesentery of the small bowel into the right iliac fossa, and in passing through the opening it had become twisted. The volvulus was reduced, and the loop of sigmoid withdrawn through the opening in the mesentery of the small bowel. The carcinoma of the splenic flexure was resected and an end-to-side sigmoido-transverse colostomy was done with the modified Furniss clamp. The patient's course was satisfactory until the 6th postoperative day, when he became somewhat apathetic, the pulse and temperature showed slight elevation to 110 and 99°F respectively, and he complained of abdominal discomfort. Examination of the recent wound revealed signs of gas bacillus infection of the second operative incision, which was subsequently proved by culture. Both the local and constitutional manifestations on this occasion were relatively mild in comparison with the first attack, and within 24 hours after opening the wound and the intravenous administration of 1 ampule (30 cc.) of antitoxin the process was obviously receding. The patient from this point made a satisfactory recovery.

The simultaneous occurrence in this case of a constricting annular carcinoma of the splenic flexure and a volvulus of the sigmoid is perhaps its most significant feature and the key to the explanation of the subsequent events. It constituted, in effect, virtually a closed intestinal loop which many investigators have shown to provide optimum conditions for the proliferation of *Cl welchii*. The

ease of control of the infection in the second wound four weeks after antitoxin had been given is noteworthy.

CASE 2. K. T., a 74 year-old woman entered the hospital April 28, 1937 with a diagnosis of carcinoma of the transverse colon. She gave a history of mild recurrent obstructive symptoms of 2 years duration and of increasing bowel frequency with passage of blood and mucus for 9 months.

On examination a freely movable tumor mass the size of a grapefruit was palpable in the left lower quadrant. A barium enema showed this to be an obstructing carcinoma of the transverse colon. After 6 days of preparation with magnesium sulfate by mouth and enemas and transfusion exploration was done. An operable carcinoma of the transverse colon was found. It was resected and an end-to-end anastomosis was done with the modified Furness clamp. A purse string type of cecostomy was done, the cecostomy tube being brought out through the omentum and through a stab wound in the right lower quadrant.

The patient's convalescence was entirely without incident until the 7th postoperative day, when the temperature rose to 102 F., and the pulse to 115. Examination of the wound showed slight edema and reddish discoloration around the cecostomy wound. At this time crepitation was not observed. By the following morning the discoloration had extended out into the flank, and had taken on the coppery red color characteristic of *Cl. welchii* infection. Definite crepitus, which could be heard with a stethoscope, was present in the tissues all about the incision.

The wound was opened up with the consequent release of a large amount of grayish-black watery discharge carrying the pungent odor commonly associated with anaerobic infection. Peroxide irrigations and dressings were begun and 1 ampule (30 cc.) of gas-bacillus antitoxin was given intravenously. This dose was repeated on the 2nd and 3rd days. The infection slowly advanced into the flank, and on the 4th day a counter incision was made in the flank, and a copious amount of the same grayish black, watery discharge and necrotic fragments of fascia were discharged. The dosage of antitoxin was increased to 2 ampules given intravenously and this amount was administered on the 5th and 6th days. At this time it became apparent that the infection was controlled. The patient showed continuous improvement and was out of bed on the 20th postoperative day and was discharged home on the 25th day.

The report on the culture in this case was somewhat equivocal being "morphologically compatible with *Cl. welchii* but not diagnostic. Nevertheless the clinical features of the disease, while not so fulminant as in our first case, were so clear cut and definite that we have no doubt whatever that it represented a gas-bacillus infection of the abdominal wall. Unfortunately, animal inoculation was not done.

DIAGNOSIS

The successful treatment of gas-bacillus infection is dependent, perhaps to a greater extent than in infection caused by any other pathogen on

early recognition and immediate institution of remedial measures. The rarity with which this type of infection occurs as a complication of abdominal surgery may lead to confusion and failure to establish the diagnosis. This delay may be fatal.

The diagnosis in the fulminating type of infection represented by Case 1 is usually made without difficulty. The process develops with lightning like rapidity, and usually occurs within twenty-four to thirty-six hours after operation. The pulse and temperature rise abruptly and the patient is in a state of severe shock, which appears out of proportion to the local findings. There is generally delirium of varying degree which may be intermittent. There is severe pain referred to the wound. The local findings, the coppery-red discoloration of the skin, the crepitation and the marked tenderness on palpation are classic and hardly require repetition. Before these signs are fully developed the characteristic odor may not be observed. It is sometimes made apparent by probing the wound, which releases a small amount of grayish-black, thin, watery discharge, with or without air bubbles. Perhaps the earliest and most helpful diagnostic sign is the crepitation, which can be heard with a stethoscope as one's fingers press the abdomen near it.

In the less fulminating type of infection represented by the second attack in Case 1 and by Case 2, the diagnosis may be more difficult to establish. The onset is usually delayed occurring about the sixth or seventh postoperative day. The toxemia is less profound, the pulse rate rises only to 110 or 120 and the temperature to 102°F or less. Local pain is less, or may be absent, and the characteristic signs of the infection are slower in developing.

TREATMENT

Certainly if one is at all suspicious of gas-bacillus infection immediate smears and cultures from the wound should be made. It is quite likely that *Cl. welchii* will be found far more frequently than one expects if more such cultures are made. While waiting for culture reports, however active treatment should be instituted at once in any patient who is suspected of having gas bacillus infection.

The radical methods of treatment so helpful in gas bacillus infection of the extremities cannot be applied when the infection involves the structures of the abdominal wall. The wound, however must be widely and freely opened by removing the skin and fascial sutures. In each of our cases only the peritoneal suture line was left intact after we had opened the wounds. We

dressings with hydrogen peroxide may be applied to the wounds and should be kept saturated with this solution. It seemed to us illogical to pack any gauze into the wounds. It appeared hopeless to make numerous counter-incisions, since the infection rapidly spreads through subcutaneous tissue, and we did not do this unless an abscess appeared.

In each of our cases we relied almost entirely on the use of large amounts of polyvalent gas-bacillus antitoxin with excellent results. In early 1937 sulfanilamide had not been proved beneficial in gas-bacillus infection, and we did not use it. We should use it today, but we should be very hesitant to omit giving the antitoxin as well. Macey¹⁰ reports a case of gas-bacillus infection which could not be controlled by sulfanilamide therapy alone but was controlled with a combination of gas-bacillus antitoxin and sulfanilamide.

Chief reliance must still be placed on early and energetic use of polyvalent antitoxin, together with wide opening of the incision, debridement of necrotic fascia and muscle and irrigation of the wound with hydrogen peroxide.

In the fulminating type of infection the dose of antitoxin, which we prefer to give intravenously, should be from 3 to 4 ampules (90 to 120 cc) daily until the infection is obviously controlled. It may be necessary to continue treatment for seven days or longer.

In the milder type of case, the dosage of antitoxin may be somewhat less—2 to 3 ampules (60 to 90 cc) daily. In Case 2, although the ultimate outcome was entirely satisfactory, we believe that the period of morbidity would have been shortened had we given antitoxin in larger dosage during the first three days.

X-ray therapy as an adjunct form of treatment has been advocated by Kelly¹⁶ and others, and Kelly suggests that benefit obtained from this form of treatment may be due to the formation of hydrogen peroxide in the tissues. He reports a series of 40 cases with a mortality of 17 per cent, which is in sharp contrast with the general mortality for this disease, in the neighborhood of 50 per cent. However, all but 2 of his cases received serum as well as x-ray treatment. On the other hand, Coleman and Bennett⁸ report 14 cases treated by x-ray alone with a mortality of 72 per cent. Probably nothing is to be lost by the use of x-ray treatment along with other measures, but expected benefit from it must not lead us into the error of any relaxation of the energy with which the more orthodox measures are used. Adequate surgical drainage, debridement and intensive use of polyvalent antitoxin still constitute the basic treatment for this disease, to which with our present

knowledge we should no doubt add the use of sulfanilamide.

SUMMARY

Gas-bacillus infection of the abdominal wall is an uncommon complication of abdominal surgery, which, however, may occur after virtually any type of abdominal operative procedure. It is seen most often as a complication of operation for gangrenous appendicitis, and is not rare after decompressing operative procedures for acute intestinal obstruction.

The causative organisms *Cl. welchii*, *Cl. oedematis maligni* and other closely related anaerobes, are widely distributed in nature and are normal inhabitants of the gastrointestinal tract of man and animals.

Under ordinary conditions these organisms, as normal inhabitants of the bowel, are innocuous and produce no absorbable exotoxin. Under obstructive conditions of the bowel the environment becomes favorable for their rapid growth and for the release of their latent toxic and invasive properties.

Two cases are reported of gas-bacillus infection of the abdominal wall complicating cecostomy done for obstructing carcinoma of the colon, with survival in each case after treatment with polyvalent gas-bacillus antitoxin. We believe that the therapy of gas-bacillus infections of the abdominal wall should today consist of free surgical drainage, antitoxin treatment and the use of sulfanilamide.

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PRIMARY STREPTOCOCCAL PERITONITIS*

Report of a Case Which Developed While the Patient Was Undergoing Sulfanilamide Therapy

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THERE has been considerable variation in the treatment of primary peritonitis in children and there has been in most instances a uniformly high mortality. We¹ recently reported an effective method of treatment of primary peritonitis as shown by a definitely lowered mortality. In that report, early operation for diagnosis of the offending organism and drainage with minimal manipulation was stressed. Specific therapy with sulfanilamide, or sulfapyridine and antipneumococcus serum, should then be started as soon as possible.¹ It is the purpose of this report to re-emphasize the present method of treatment of primary peritonitis, and to present the information gained from an unusual case of primary streptococcal peritonitis.

REPORT OF CASE

E. G., a white boy aged 9 years entered the Medical Service of the Children's Hospital Boston March 15, 1939 complaining of a painful swelling in the neck of 6 days duration. Twenty-two days before entry the patient's right ear was painful and spontaneously began to discharge thin yellow pus which continued until 6 days before entry. At this time, the left side of the neck became swollen and tender. This was associated with daily shaking chills and fever. Three days before entry he began to vomit everything given by mouth.

There was no family history of tuberculosis, syphilis, diabetes or blood diseases. The patient's health had always been good except for whooping cough at the age of 4.

On physical examination the patient was a well developed thin boy who appeared acutely ill. The anterior cervical nodes on the left were moderately enlarged, indurated and tender. There was no other adenopathy. Examination of the throat was not remarkable. The left

cardium was dull gray and the landmarks were obliterated. The right cardium was tense and bulging posteriorly. There was tenderness over the left mastoid. The heart and lungs were normal. The abdomen was not tender and there were no masses or spasm. Rectal examination was normal. The rectal temperature was 100.4 F and the pulse 72.

Examination of the blood showed a red-cell count of 3,280,000 with 70 per cent hemoglobin (Sahli) and a white-cell count of 25,400 with 95 per cent polymorphonuclears, 5 per cent lymphocytes and 2 per cent large monocytes. The urine contained a large trace of albumin and 20 to 30 red-blood cells and 3 to 4 granular casts per high-power field. The serum nonprotein nitrogen was 133 mg per 100 cc. and the serum protein 5.9 gm. The throat culture grew many hemolytic streptococci. When he was admitted to the hospital he gave the impression of bilateral otitis media, bilateral mastoiditis and acute hemorrhagic nephritis.

Sulfanilamide, 1½ gr per pound was started the same day. The day of entry roentgenograms of the mastoids revealed bone destruction on the right. Paracentesis of the right cardium was performed the day of entry with the release of a small amount of bloody fluid. On March 18, 2 days after entry the blood level of sulfanilamide was 15 mg per 100 cc. The patient's temperature was normal and he seemed improved until March 19 when he complained of generalized abdominal pain for the first time and his temperature rose to 101 F. Eighteen hours after the onset of the abdominal pain a diagnosis of generalized peritonitis was made. Incision and drainage of the peritoneal cavity was then performed under local anesthesia. A large amount of thin greenish pus was obtained from which a beta-hemolytic streptococcus was cultured. A large amount of pus drained from the abdomen for 7 days following operation. The patient's temperature continued to be elevated between 101 and 102 F daily. On March 22 a right mastoidectomy was performed but the culture of the pus obtained did not grow any organisms. The blood level of sulfanilamide varied between 26 and 10 mg. per 100 cc. until March 30. During this time the serum nonprotein nitrogen decreased to 29 mg per 100 cc. and there were fewer red blood cells in the urine. Nine days after the abdominal operation the drain was removed and the wound healed in the next 3 days. The mastoid wound was healed 10 days after operation. The nodes in the neck had subsided by this time.

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*Primary peritonitis (no known or identifiable metastatic peritonitis) or secondary peritonitis that is not secondary to inflammation or ruptured hollow viscus. The offending organism in children most commonly hemolytic streptococcus or pneumococcus.

On March 23 physical examination revealed signs of pneumonia at the left base. This was confirmed by a roentgenogram of the chest. A blood culture taken on March 20 was positive for hemolytic streptococcus, but several subsequent blood cultures were negative for the same organism. The red-cell count fell to 2,780,000 and numerous blood transfusions were given during his hospital course. The white-cell count remained elevated between 25,000 and 50,000.

Signs of fluid gradually appeared in the left chest, and on April 11, a blood culture was positive for *Staphylococcus aureus*. On April 13 resection of a portion of the 8th rib on the left was performed. A large amount of pus was obtained from which a beta hemolytic streptococcus and *Staphylococcus aureus* were cultured. Sulfanilamide therapy was started again on April 4 and discontinued on April 13. The blood level of sulfanilamide during this period varied between 80 and 135 mg per 100 cc.

After the rib resection, the patient's temperature started a downward trend, but 5 days later it again started to spike between 101 and 104°F daily. On April 23 the left chest was re-explored, with release of more pus, from which a hemolytic streptococcus was cultured. Roentgenograms of the chest showed the heart to be markedly displaced to the right at this time. The patient's course continued to be stormy and he became very edematous. The serum protein was 45 gm per 100 cc. on May 1. On May 2 two pericardial taps were performed and a total of 700 cc of pus was obtained, from which a hemolytic streptococcus was cultured. On May 3 a pericardiostomy was performed under local anesthesia and about 1000 cc. of streptococcal pus was drained. The patient's condition improved slightly after this but soon became worse, and death followed 18 hours after the pericardiostomy. Shortly before death, aspiration of the right chest produced 650 cc of thin streptococcal pus. Roentgenograms taken several hours previously had shown no evidence of fluid in the right chest.

Autopsy An autopsy was performed 8 hours postmortem. The anatomical diagnoses were hemolytic streptococcus septicemia, bilateral hemolytic streptococcus pleuritis, hemolytic streptococcus pericarditis, bilateral bronchopneumonia, generalized lymphadenopathy and peritonitis (healed). There were numerous filmy fibrous adhesions between loops of intestine. There was a small localized abscess (5 cc.) in the right lower quadrant, which was sterile on culture. The appendix showed no evidence of inflammation. It was the impression at the time of performing the autopsy, 45 days after drainage of the peritoneal cavity, that the peritonitis was healed.

There are several significant points about the foregoing case. The patient entered the hospital with manifestations of a streptococcal infection which was confirmed by positive throat cultures. Sulfanilamide therapy was started immediately. The blood level of the drug was 78 mg per 100 cc on the second day, 98 mg on the third and 149 mg on the fourth. The patient seemed somewhat better and his temperature was normal, despite the clinical improvement and the four days of sulfanilamide therapy, the patient developed signs of generalized peritonitis. Recurrence of spread of streptococcal infection does occur when the dosage of sulfanilamide is stopped or diminished,³ but is unusual when the drug is at an optimum blood level,⁴ as in this case.

The problem then arose. Should the sulfanilamide therapy be continued alone or should it be reinforced by incision and drainage of the peritoneal cavity? The latter course was decided on, and within eighteen hours after the onset of the symptoms of peritonitis, a small incision was made under local anesthesia in the right lower quadrant. A large amount of thin greenish pus containing flecks of fibrin was released and a pure culture of a beta-hemolytic streptococcus was obtained. The wound drained a large amount of pus for about seven days. We fully realize that it is impossible to drain the entire peritoneal cavity, but this case and others¹ have demonstrated that drainage does remove considerable amounts of pus. After the operation, the dosage of sulfanilamide was increased so that the blood level was 223 mg per 100 cc the day after operation. The signs of peritonitis gradually subsided so that by nine days after operation the abdomen was negative to physical examination. The drain was removed on that day, and the wound rapidly healed.

The right mastoid was operated on three days after the peritoneum was drained, no organisms were recovered. The patient's nephritis improved, as judged by the lowered serum nonprotein-nitrogen levels. However, pneumonia developed in the lung and was complicated by empyema, from which both *Staphylococcus aureus* and a beta-hemolytic streptococcus were obtained on culture. Sulfanilamide therapy was stopped fifteen days after entry because despite high blood levels the infection was not under control. The empyema was drained, and then the patient developed a hemolytic streptococcus pericarditis. This was also drained but the patient died the same day, which was fifty days after entry.

Examination of the peritoneal cavity at autopsy revealed no evidence of active peritonitis. There were numerous adhesions and one pocket containing a small amount of sterile exudate. From a clinical and anatomical viewpoint, the peritonitis was healed. The pericardial and pleural cavities revealed evidence of widespread infection. No unrecognized focus of infection was found.

The outstanding feature of this case is that the whole train of disease processes due to a beta-hemolytic streptococcus developed while the patient was receiving large amounts of sulfanilamide. The peritonitis responded to treatment very well, and despite the pulmonary and pericardial complications, this fact is further favorable evidence that primary peritonitis due to the streptococcus should be treated by early operation so as to identify the offending organism and drain the peritoneal cavity. Sulfanilamide therapy

should be started as soon as the organism obtained at operation can be identified as a streptococcus by smear and culture.

SUMMARY

A case of primary streptococcal peritonitis, which developed while the patient was undergoing sulfanilamide therapy, is reported.

Early drainage of the peritoneal cavity is emphasized as an important aid in the treatment of streptococcal peritonitis.

Sulfanilamide is a valuable therapeutic agent

but does not always prevent spread of infection even with optimum blood levels, and other methods of treatment should not be discarded for sulfanilamide alone

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LABORATORY DIAGNOSIS OF ENCEPHALITIS DUE TO THE EQUINE VIRUS*

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BEGINNING early in August, 1938 cases of encephalitis began to occur in southeastern Massachusetts which have been proved to be due to a virus^{1, 2} which had not heretofore been known to cause disease in man. The new etiologic agent is the Eastern virus of equine encephalomyelitis, which, beginning in 1934, was recognized as the cause of disease in horses in several states along the Atlantic seaboard.

RÉSUMÉ OF CASES IN 1938

During the late summer and fall of 1938, over 50 cases of illness, suspected to be due to this virus, came under investigation by this department. Some of these cases have been proved to be caused by other etiologic agents, but in 34 cases there is reason to believe that the equine virus was the cause of the illness. Nineteen of the patients were under five years of age, and 5 were under ten. This high incidence in the younger years of life is in direct contrast to the St. Louis outbreak of encephalitis, in which those in the older age groups were most frequently attacked.

Of the 34 cases, the equine virus was isolated from the brain tissue of 9 fatal cases. Neutralizing antibodies for the virus were found in the blood of 10 cases in which the patients survived. The diagnosis has therefore been definitely proved in 19 cases. The etiology of the remaining cases is not so well established. In 9 fatal cases the pathologic picture was so characteristic that there is reason to believe that these cases were due

to the same etiologic agent. In 6 additional fatal cases the clinical picture was sufficiently similar to that seen in the proved cases as to indicate the same causative agent.

At the same time that the human cases were being discovered, an epidemic among horses was present in the same area. By the end of the season nearly 300 deaths among horses, reported to have been due to encephalomyelitis, were brought to the attention of the Massachusetts Division of Livestock Disease Control. The highest incidence in human beings occurred early in September approximately a week after the highest incidence among horses. Further information in regard to the outbreak will be found in a report³ presented to the American Public Health Association in October, 1938. Encephalitis in human subjects due to equine virus has already been discovered in three other states. Undoubtedly cases will eventually be discovered in the other states in which the disease is prevalent among horses.

MOSQUITO TRANSMISSION OF DISEASE

Laboratory and epidemiological evidence points to the fact that the virus is transmitted by mosquitoes. As early as 1933 Kelser⁴ demonstrated that mosquitoes could transmit the disease from guinea pig to guinea pig in the laboratory and since that time it has also been transferred to horses by the bite of certain mosquitoes. Until recently it was supposed that the disease was limited largely to horses but it now appears that the virus is probably harbored by other animals, including certain birds,^{5, 6} such as pigeons and pheasants. The present opinion is that these other animals are the primary reservoir and that man and horse are merely secondary hosts which ac-

*Presented at the annual meeting of the Massachusetts Medical Society June 7, 1939.

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identally become infected by mosquitoes which have previously bitten the animals harboring the virus

Because it seems quite clear that the disease is carried by mosquitoes, prevention of the spread of the disease by eliminating the varieties of mosquitoes which can carry the virus seems to be the most hopeful method of control. So far only mosquitoes belonging to one family (*Aedes*) have been able to act as the biological host of the virus. In all other varieties the virus promptly dies in the intestinal tract of the mosquito and cannot be obtained after two or three days have elapsed following the feeding upon an infected animal. This would indicate that control measures could be limited to particular varieties of mosquitoes. Of the members of this family which have so far been incriminated, the following have been reported to be present in Massachusetts: *Aedes sollicitans*, *Aedes cantator*, *Aedes vexans*, *Aedes taeniorhynchus* and *Aedes dorsalis*.

MOSQUITO SURVEY OF MASSACHUSETTS

If we can profit by the experience gained in the control of malaria and yellow fever, it is believed that much more can be accomplished by directing control measures against the worst-offending varieties instead of against the whole mosquito population. To carry out such selective control, it is necessary to know where the *Aedes* mosquitoes are breeding. This information is being obtained in a mosquito survey sponsored by the department during the present season. More than one hundred field workers furnished by the Works Progress Administration are collecting specimens in all parts of the State. In addition, numbers of volunteer collectors have been enlisted who will obtain specimens around their own homes.

LABORATORY CONFIRMATION OF DIAGNOSIS

The only way in which a diagnosis of encephalitis due to the equine virus can be made is by laboratory procedures. Clinically the disease is the same as any other encephalitis except that it tends to be more fulminating, has a shorter course and is characterized by a high fatality rate. One helpful point is the fact that early in the disease the cell count in the spinal fluid is not especially high (usually 200 to 1000 cells per cubic millimeter) with a preponderance of polymorphonuclear leukocytes during the first two or three days of the disease, but with a rapid reversion to a preponderance of mononuclear cells as the count later decreases.

Unfortunately an etiologic diagnosis is not possible during the first four or five days of the ill-

ness, because at that time the virus is inaccessible, as it is present only in the brain tissue, and neutralizing antibodies for the virus have not yet appeared in the blood stream. It has not yet been demonstrated how early these antibodies appear in the blood. Therefore, a 10-cc sample of blood should be obtained as soon as a diagnosis of an encephalitis not clearly due to some other agent is made. It may eventually be discovered that neutralizing antibodies are present well before the end of the first week of illness. Since the virus is not found in the spinal fluid after the onset of symptoms, specimens of spinal fluid should not be sent in for virus examination.

From the public-health point of view it is important to establish an etiologic diagnosis, since the institution of control measures will begin as soon as a case has been discovered.

SPECIMENS TO BE OBTAINED

Since death often occurs within twenty-four to forty-eight hours after the case is first seen by the physician, the only way by which an etiologic diagnosis can be made on fatal cases is to isolate the virus from brain tissue removed post mortem. For virus isolation, the tissue must be placed in a neutral solution of 50 per cent glycerin made up in physiological salt solution. This solution will preserve the virus until it reaches the laboratory. Such a specimen should be mailed or sent by messenger to the Department of Bacteriology at the Harvard Medical School.

Further important information can be obtained by examining microscopic sections of the brain and cord. Pathologists connected with local hospitals are usually prepared to make such sections but if such facilities are not available, the brain and cord should be preserved in 10 per cent formalin and sent to this department.

If the local pathologist has not had an opportunity to study microscopic sections of fatal cases of this disease, the department can make arrangements for him to see the material which has been accumulated in the pathological departments of the three large medical schools in Boston. In addition, the department has requested Dr. Sidney Farber, of the Children's Hospital and the Harvard Medical School, Dr. Charles F. Branch of the Massachusetts Memorial Hospitals and Boston University and Dr. Harold E. MacMahon of Tufts College Medical School to act as a committee of consultants. They have agreed to lend assistance to the pathologists of the State in examining any material which may be suspected of being from a case of encephalitis due to the equine virus.

Where the patient survives as long as four or five days, or where complete recovery takes place, a 10-cc. sample of blood taken under aseptic precautions and put into a sterile tube should be mailed or sent by messenger with accompanying information in regard to the case, to Dr Leroy D Fothergill at the Department of Bacteriology of the Harvard Medical School where examination for neutralizing antibodies will be made. When a sample has been obtained early in the disease, another sample should be obtained during the ensuing week, unless some other diagnosis has been made in the meanwhile, in order to make sure that at least one sample will be taken at a time when neutralizing antibodies can be expected to be at a high titer. As noted above, the virus cannot be isolated from spinal fluid and such specimens should not be sent in for this purpose.

The department has made arrangements to take care of the examination of specimens from any cases in which a presumptive diagnosis of encephalitis is made but if specimens come in from a wide variety of cases in which such a diagnosis

has not as yet been made it may result in more specimens being received than can be examined, since the procedures are both expensive and time consuming. The co-operation of physicians is therefore requested in limiting specimens to those cases in which a presumptive diagnosis of infectious encephalitis is made. It is not believed that a case which does not show a rise in temperature to at least 102°F can be due to the equine virus. In addition to the fever, there should be distinct signs of cerebral irritation, such as the presence of spasmodic contractions or actual convulsions or of marked stupor or coma.

State House.

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REPORT ON MEDICAL PROGRESS

CONTAGIOUS DISEASES

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SCARLET FEVER

SCARLET FEVER is a disease caused by a group of beta hemolytic streptococci capable of producing a soluble toxin. Only those individuals who are susceptible to the toxin react to this infection with a rash, the non-susceptibles showing only sore throat and fever. Most children are susceptible to the toxin. Therefore, in them the infection usually produces a rash. One attack of the disease usually affords a lifelong active immunity but such immunity is confined to this particular group of toxin-producing streptococci and not to other streptococcal diseases. Relapses are thought to be due to reinfection with another strain before a polyvalent immunity to all scarlet fever strains has been established.

Hospitalization by municipal decree of all cases of scarlet fever for four weeks has not controlled

the incidence of the disease in Stockholm, but this has been accompanied by a lowering of the mortality rate.¹ Reduction of the isolation period of uncomplicated cases from four weeks to three has proved satisfactory in certain localities in the United States. In fact it has been found safe to release adults in the summer months at the end of two weeks. Any suppurative process in the nose, ear or a wound contraindicates such release unless the absence of scarlet fever streptococci can be proved by cultures and skin tests on Dick positive individuals. Such service can only be obtained in certain laboratories. Release cultures in uncomplicated cases have proved of no value, as return cases are just as apt to occur from those with negative as from those with positive cultures. Finally Bergen in Norway and Aberdeen in Scotland have gone so far as to remove simple scarlet fever from all legal restrictions leaving it to the attending physician to report the case and handle it as a case of erysipelas as handled in Massachusetts. There is something to be

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said in favor of all these methods, and the results are being watched with great interest

The treatment of scarlet fever has been greatly advanced through the use of convalescent serum³ and the Dick antitoxin. Either of these, administered intramuscularly or intravenously within the first two days of the onset of the rash in adequate dosage, according to the age of the patient and the severity of the disease, will usually blanch the rash, reduce the sore throat and cause an abrupt fall of the temperature. Incidentally, the incidence of suppurative complications will be somewhat reduced in proportion to how early the serum is given⁴. Convalescent serum rarely gives rise to serum reactions, and the new concentrated and refined antitoxin has reduced the incidence and severity of horse-serum sickness. Serum treatment is unnecessary in mild cases and ineffective in the complications.

Sulfanilamide given in the usual dosage during the initial fever period does not reduce or shorten the fever, nor does it reduce the incidence of subsequent complications⁵. If given over a longer period it appears to reduce the incidence of complications, but clinical experiments in this longer method have not been carried out with the same care in the way of controls as were the earlier series in which the drug was used only during the fever. Furthermore, the longer the drug is used, the greater is the danger of its untoward effects. Usually these can be controlled by the discontinuance of the drug, but sudden severe anemia requires transfusion. Until a fair balance sheet is produced in regard to the beneficial protective action of this drug given as a routine over the longer period with the ill effects carefully weighed, it would seem best to recall that the early routine use of antitoxin in this disease resulted in more days of illness as a result of serum sickness than would have occurred without such treatment.

The great value of sulfanilamide in scarlet fever lies in its effect on two highly fatal complications, namely bacteremia and meningitis. In these two conditions this drug has greatly reduced the mortality and as such has materially reduced the mortality of scarlet fever, because, in New England deaths in this disease are largely due to one or the other of these two causes.

The advisability of removing badly diseased tonsils after the third week appears to have gained favor, in spite of all theoretical reasons to the contrary. The diet in scarlet fever should be the same as in any other febrile condition, and after the fever is past the diet should be the same as that for any normal individual according to age. Nephritis is no longer considered to be the result

of improper diet but of by-products elaborated by the streptococcus.

Scarlet fever can be controlled by active immunization with the toxin⁶. This has been repeatedly proved by the immunization of pupil nurses before they go on duty on scarlet fever wards. The immunity conferred is comparable to that afforded by an attack of scarlet fever. Apparently this does not result in an increase in carriers. Children can be protected in the same way⁷. This procedure has fallen into disrepute because of the large doses recommended in the past by the holders of the Dick patent, and inscribed on the commercial packages at their direction. Fortunately, the patent is soon due to expire, which will be a boon to investigative work in this disease. The administration of three doses of the "toxoid" supplied by the Massachusetts Department of Public Health has produced little or no ill effects and also a relatively low grade of immunity⁸. Until the antigenic quality of this product is improved it is not to be recommended. However, such improvement is unlikely while the Dick patent is in force⁹.

DIPHTHERIA

In recent years there has been a wave of severe diphtheria in parts of Europe, England and South America, and in these outbreaks approximately 10 per cent of the cases have been of the malignant type. From a bacteriological standpoint these severe cases are largely due to a highly pathogenic strain, endowed with the property of rapid penetration into the tissues and of producing a relatively large amount of toxin. From a practical point of view these cases present the same clinical problem as an ordinary or weakly pathogenic strain in a highly susceptible individual. Indeed, a strain of high pathogenicity is not always associated with clinical severity¹⁰. Consequently, it is best to use the term "malignant" in the clinical sense for any highly toxic case of diphtheria. Furthermore, it is well to bear in mind that the usual antitoxin is capable of neutralizing the toxin of both strains.

The Manzulla test for diphtheria consists of applying with a cotton swab a 2 per cent aqueous solution of potassium tellurite to the suspected throat lesion. In the presence of diphtheria the lesion turns black. While not infallible, the test appears to be very helpful in making a rapid bedside diagnosis¹¹. Mueller's¹² studies on the metabolic requirements of the bacillus have led to luxuriant growths on special culture media.

The following experiment explains the essence of what can be expected from antitoxin. If a standard unit of diphtheria toxin is injected

into a guinea pig of a certain weight, the guinea pig will die, but if within fifteen minutes this guinea pig is given a unit of antitoxin, the toxin will be neutralized and the animal will suffer no ill effects. However, this dose will not suffice if given later. In fact, if we wait two hours and a quarter, a dose one thousand times as great will not save the animal. When we realize that 1000 units of antitoxin to a guinea pig corresponds to 100,000 units for a fifty-pound child, we can easily understand why enormous doses of antitoxin so often fail to save malignant cases. The time element, therefore, is of the utmost importance, and in rapidly fulminating cases every hour counts. Thus, when it comes to the dose of antitoxin to be administered, the question is comparable to how much water it takes to put out a fire. However, the following table may be used as a guide.

Recommended Dose of Antitoxin

WEIGHT OF PATIENT	TYPE OF DISEASE		
	MILD	MODERATE	MALIGNANT
Under 50 lb.	5,000	10,000	50,000
Over 50 lb.	10,000	20,000	100,000

In severe cases the intravenous route is preferable, but this may be combined with the intramuscular route. A single dose may be sufficient but in severe cases additional doses are often given.

The toxemia itself produces an apathy, listlessness and finally stupor, but if the membrane and edema obstruct respiration, restlessness becomes prominent. In several contagious hospitals it is now the rule to avoid all opiates during this stage because sedative drugs mask this restlessness, which at times may be caused by a small piece of loose membrane which can be easily removed by suction. In fact, suction can sometimes obviate the necessity of intubation. This toxemia is simply a very marked form of the toxemia found in other acute infectious diseases. Dehydration often occurs as the result of difficulty in swallowing. The carbohydrate metabolism is disturbed and a vascular collapse is threatened. Intravenous dextrose (glucose) 10 per cent is indicated in all but mild cases. The addition of insulin has not been shown to be effective.¹³

In the convalescent stage—that is, when the membrane is receding or after it has entirely disappeared—myocarditis may become evident. Every type of cardiac irregularity may occur but a gallop rhythm and evidence of heart block are ominous signs, of which the latter is the more serious. The electrocardiogram may show a high degree of block before this is suggested by clinical ob-

servation. Advanced block may occur suddenly and proceed rapidly. The contractile fibers may also be involved, as shown by inversions of the T wave in all three leads, but often there is a combination of damage to the specialized conduction system and of injury to the myocardium in general. It is thought by many that drugs of the digitalis group are contraindicated since they might tend to promote block. One has but to appreciate the pathology of a diphtheritic myocarditis to understand the futility of the various drugs employed.

During convalescence vascular collapse of a different order from that seen in the toxic stage may take place. This is brought about as part of the postdiphtheritic polyneuritis, and is due to a paralysis of the motor end plates of the splanchnic vessels. This results in a marked engorgement of the splanchnic vessels with marked pallor of the skin, epigastric pain and vomiting. This usually supervenes on myocarditis and therefore throws a burden on an already damaged heart. Adrenalin is not powerful enough to overcome this condition, but Pitressin (beta hypophamine) may be helpful. Warmth from an electric light bulb under a tent is sometimes helpful. A prolonged rest in bed of six weeks is indicated whenever a diagnosis of myocarditis has been established. Needless to say, the place for the care of all cases of diphtheria—except the mild forms—is a hospital equipped with the proper facilities.

The control of diphtheria can be achieved through immunization with the toxoid or with toxin antitoxin. The best results appear to have been obtained by three doses at four week intervals.¹⁴ One dose of the alum precipitate has given the poorest results, but this method has been recently modified by following it with three to six nasal installations seven days apart.¹⁰ When diphtheria raged in New England the greatest number of cases and the highest mortality took place in children below the school age. Therefore, early immunization is desirable. Control, like the treatment, of diphtheria consists primarily of sound, protective measures applied early.

MENINGOCOCCAL MENINGITIS

The meningococcus has been shown to be a frequent inhabitant of the nasopharynx of healthy individuals. Thus, in groups enjoying good health the carrier rate has been reported from 2 per cent to as high as 54 per cent, with no cases of cerebrospinal meningitis occurring in these groups.¹⁵ It was formerly held that the carrier rate increases with an outbreak of the disease. The studies of Kuhn¹⁶ at two CCC camps in Missouri do not substantiate this theory. In one

camp, in which 9 cases of the disease occurred, positive cultures of the meningococcus from the nasopharynx were found in 44 per cent of the men, while in another camp twenty miles distant, where there were no cases, positive cultures were obtained in 35 per cent. When one considers that positive cultures were obtained in as high as 54 per cent in a group of healthy individuals without the presence of a single case it becomes clear that taking cultures of contacts is of very doubtful value as a control measure.

Another theory which has had to yield to the results of investigations is that the type of organism gives some clue to its virulence. We now know that all four types of the meningococcus may be virulent and cause serious outbreaks.¹⁰ Furthermore, by typing all cases of the disease over a period of years it has been found that one type may be superseded by another in its predominance. In this the disease differs from pneumonia.

Antimeningococcus serum is polyvalent and thus contains agglutinating properties for all four types. Its efficacy depends on how early it is administered and how often it is administered as well as on the dose. Without serum the mortality was 80 per cent. In cases treated early with the serum the mortality is now between 6 and 20 per cent. Sulfanilamide appears to be effective in this disease, both alone and more especially in conjunction with serum treatment.^{17, 18}

WHOOPIING COUGH

In Massachusetts 80 per cent of all the deaths from whooping cough occur in the first year of life and 96 per cent occur in the first two years. The newborn appear to lack that relative immunity which they have for measles, mumps, scarlet fever and diphtheria. Therefore, every effort should be made to protect them from exposure. Bronchopneumonia is the commonest complication and often results from additional infections such as influenza, measles and common colds. Encephalitis may result from a superimposed latent neurotropic virus.¹⁹ In rare cases convulsions are the result of tetany, but for the most part they are due to inefficient cerebral circulation during paroxysms.²⁰ These may be diminished by an oxygen tent and by barbiturates. The neurologic complications have been reviewed by Eley.²¹ The heart is not permanently injured by the paroxysms.²²

The early clinical diagnosis of whooping cough is generally made on the circumstantial evidence of exposure and an afebrile, paroxysmal and spasmodic cough which increases in severity and is generally worse at night. The white-cell count shows a gradually increasing leukocytosis with a high

lymphocyte percentage. Cough droplet cultures yield *Hemophilus pertussis* in about 80 per cent of cases in the catarrhal stage, 60 per cent in the first week of the paroxysmal stage, 30 to 35 per cent during the second week, 15 to 20 per cent in the third week and 2 to 5 per cent in the fourth week. In keeping with this, it was found that in 70 per cent of whooping cough cases the patients were infected by exposure to individuals in the catarrhal stage.²³

The present status of pertussis vaccine in the prevention of whooping cough has been reviewed by Maxcy.²⁴ He shows that up to 1931 the available evidence failed to establish the prophylactic efficacy of vaccines. Since then, however, progress in the cultivation of *H. pertussis* has resulted in the production of vaccines with definite immunizing power more in line with those of other antigenic agents of well-recognized value. The etiologic relation of *H. pertussis* to whooping cough has been firmly established,²⁵ and it has been shown that this organism in the course of cultivation undergoes changes during which its antigenic element, toxicity and infectiveness diminish markedly. Only in its primary, fresh smooth phase is it effective for immunizing purposes. This explains the variable and unsatisfactory results obtained in the past. Sauer²⁶ has used these fresh preparations in total doses of 70,000,000 to 80,000,000, or four times greater than those previously employed with results which leave no doubt as to its efficacy as a preventive. Maxcy's excellent and critical review of the results obtained by Sauer and others with this new preparation deserves scrutiny by those whose opinions of the merits of pertussis vaccine date back to its previous doubtful status.

Maximum protection is not to be expected until about four months after the completion of three or four bilateral subcutaneous injections of Sauer's vaccine at intervals of one week.²⁷ It should be kept in mind that such protection is not absolute but relative. Furthermore, on this basis little if any value can be expected from this measure as a preventive after exposure has taken place, to say nothing of when the disease is already under way.

The difficulties at present lie in the fact that there is no reliable method of standardization, consequently the dosage remains arbitrary. Furthermore, the antigenic substance contained in this newer preparation has not yet been identified. Consequently, commercial preparations are apt to vary in their potency. The most severe reactions are unfortunately apt to occur in very young infants, the very ones who need protection most. A severe reaction, however, is not so dan-

gerous at this age as is a severe attack of whooping cough

MUMPS

In 1934 and 1935, Johnson and Goodpasture²¹ established that mumps is caused by a filterable virus. This virus was obtained from the fresh saliva of mumps patients during the first two days of the parotid swelling, as determined by transfer to monkeys through injection of the parotid duct and back again to infect non immune human volunteers through spraying the mouth.

Silver⁹ in 1936 and Finkelstein²⁰ in 1938 confirmed the findings of previous French observers of a latent encephalitis in the course of mumps. This consists of the finding of varying numbers of lymphocytes in the spinal fluid without any clinical signs or symptoms to suggest the presence of meningoencephalic involvement. The cells counts in these cases ranged from 11 to 890 cells per cubic millimeter. I have recently seen a case of this kind with a cell count of 400. The frequency with which this occurs is unknown because routine punctures are not done in this disease. The fact that it does occur is evidence of the mildest form of neurotropic activity of a virus.

Clinical evidence of mumps encephalitis appears to be present in almost 10 per cent of adult cases, but the great majority of these are mild in character. It is indistinguishable from the condition found in preparalytic poliomyelitis except by the circumstantial evidence of the existence of mumps. Only rarely does it produce severe symptoms. The treatment is lumbar drainage.

Severe orchitis may be helped by early incision of the tunica albuginea bringing about a rapid fall of a high fever, and apparently avoiding subsequent atrophy as determined by follow-ups.²¹ Owing to the long incubation period, mumps convalescent serum is very effective as a preventive if administered within the first week after exposure, but such passive immunization is of short duration.* Statistics fail to give convincing evidence that complications are reduced when the serum is administered after the disease is in progress.

MEASLES

An important step in the prevention of measles has been the development of human placental immune globulin by McKhann.²⁻²³ Progress is being made in the effort to improve this product whereby its ill effects will be minimized and its potency stabilized. Karelitz²³ recommends the globulin fraction of immune adult serum. When

these are brought to a satisfactory stage in commercial development they bid fair to replace the use of convalescent serum and adult immune serum. All these materials are now being used to prevent or modify the disease. The protection afforded by them is of short duration, but it is of distinct value for two or three weeks. In order to prevent the disease they must be given within a few days of exposure. In order to modify it they must be given approximately one week after exposure, and modification cannot be expected in all cases so treated. The advantage of modification lies in the apparent permanent immunity.²⁷ After all, measles is a good hurdle to get over and if the patient is over four years of age and healthy it is not to be dreaded. Circumstances however, often make prevention or modification desirable.

POLIOMYELITIS

The researches of Aycock into the epidemiological characteristics of poliomyelitis indicate that it is due to a rather widespread virus infection of the upper respiratory tract which may involve the gastrointestinal tract. Like the meningococcus it gives rise to characteristic symptoms only when it gains access to the nervous system. This theory implies that there must be carriers among the population but also that the great majority of the population become sooner or later immune through unrecognizable attacks.

There is no reliable specific serotherapy for poliomyelitis. Convalescent serum has never been established as of value once the disease is in progress, either in the preparalytic or paralytic stage.²⁸ If an immune serum could be so concentrated that much greater doses were possible than those now available some benefit might be expected. This does not mean that we should refuse serum if it is demanded, because, after all, the medical profession is entirely responsible for the present demand. Violent opposition to an impetus of this magnitude is dangerous.

Two methods of control have been attempted in the past five years. One of them has been to give subcutaneous injections of the virus.²⁹ If dead virus was injected no specific resistant response followed. On the other hand if the virus was alive, even though attenuated such injections sometimes were followed by the disease itself.³⁰ While the spraying of zinc sulfate, picric acid and alum appears to afford some protection to monkeys from the experimental disease, there is no good evidence that this method has been protective against the natural disease in human beings. The possibility of injury to the nasal mucous membrane by these chemicals might well

*Convalescent sera of this kind can be purchased and obtained by air mail from the Manhattan Serum Co. in New York City (Dr. William Thellusier, director).

break down those important barriers to infection, and subsequently open the way to sinus infection and possibly to central-nervous-system involvement of this or other infectious agents inhabiting this area. Until a non-injurious, specific, chemical agent is found, it would appear wise to explain our limitations to those who turn to us for guidance.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25431

PRESENTATION OF CASE

A thirty nine year-old Russian-born Jewess was admitted to the hospital complaining of pains and swelling in the extremities and of cough

The patient stated that she had always been well and active until eight months before admission when, while working as a clerk in a department store, she was suddenly seized with a constant, non radiating sharp pain in the calf of the right leg while standing. She continued to work for the remainder of the day. She returned home and went to bed, where she remained for five to seven weeks under the care of a physician. The latter stated that the leg was swollen from ankle to knee and that it was tender especially along the course of the superficial veins, which felt "hard, like cords." She improved slowly and six months before entry returned to work. Ten days later, however a severe sharp pain was noted in the right chest, which was made worse by breathing. She again went to bed and three or four days afterward developed a hacking cough productive of about a fourth of a cupful of thick, yellowish, non foul smelling occasionally blood flecked sputum. This cough and chest pain persisted for about three months, but three weeks later the tissues and lymph nodes in the right half of the anterior neck became swollen and markedly tender. The neck veins became enlarged, dark blue firm and "cord like," but disappeared in three weeks. The right arm and left leg became similarly involved, so that they were swollen, tender and faintly cyanotic, and the palpable veins "cord like." These symptoms slowly subsided until six weeks before admission, when the patient, still afebrile, noted an increase in the severity of her cough so that she had paroxysms with the raising of foul-smelling, heavy yellow, rarely blood flecked sputum which nauseated her and occasionally caused her to vomit. Furthermore, she stated that the right chest pain which she had previously experienced was stabbing, aggravated by cough, and located in the right infraclavicular region. She said that x-ray films taken in an outside hospital six weeks before entry showed findings interpreted as being an "infarct." Two weeks before admission the patient thought that

the ends of her fingers had become larger. During the present illness she was reported to have gained 16 pounds in weight. At no time had she experienced night sweats or fever. The patient further stated that she had had mild previously asymptomatic varicose veins for several years.

Her family history was noncontributory.

Physical examination revealed a slightly obese, tanned woman who was coughing up blood stained sputum at frequent intervals. There were a few, almost healed psoriatic lesions over the right ankle and forearm. The right pupil was larger than the left. The throat was slightly injected. In both supraclavicular regions and in the left posterior triangle, were numerous tender nodules 0.3 to 2.0 cm. in diameter. The supra-sternal dullness was slightly widened. Examination of the heart was negative. Examination of the lungs showed questionable amphoric breathing over the region of the right middle lobe. There was a moderate degree of clubbing of the fingers. The veins of the volar surface of the left forearm were tender and apparently thrombosed. There were very mild varicosities of the legs. There was no residual brawny swelling anywhere. A rectal examination showed only small internal thrombosed hemorrhoids. Nothing abnormal was felt in the pelvis. The menses were virginal.

The temperature was 99°F., the pulse 88, and the respirations 24.

Examination of the urine on many occasions was essentially negative. The blood showed a red-cell count averaging 4,700,000 with 70 per cent hemoglobin and a white-cell count which averaged 25,000 with 85 per cent polymorphonuclears. The stools were guaiac negative. Sputum culture showed a heavy, practically pure growth of monilia. A blood culture and Weil-Felix acid undulant fever agglutination tests were negative. A blood Hinton test was negative. The electrocardiogram showed a ventricular rate of 75, with normal rhythm upright T₁ and T₂ with flat T₃ and a tendency to low voltage. X-ray films of the chest revealed scattered areas of consolidation throughout both lung fields, which were confluent in both middle lung fields, particularly in the right middle lobe and in the anterior portion of the right lower lobe. In the left lung field there were multiple, round poorly defined areas of increased density. Films of the hands showed slight soft-tissue swelling about the terminal phalanges but the bones showed no evidence of osteoarthropathy. A gastrointestinal series was negative.

On the day after admission the temperature rose to 100.5°F., and remained at about this level throughout her stay. On the eleventh hospital day after leading an uneventful hospital course, she

developed thromboses of two superficial vessels in the calf of the right leg, which were biopsied. Anaerobic and aerobic cultures were negative, the small vessels removed showed acute thrombophlebitis. Subsequently, at varying intervals, smaller lesions appeared on the wrists, arms and thighs. The patient slowly but steadily became weaker, and despite digitalization her edema persisted. Additional x-ray films of the chest showed no significant changes from those previously observed. One month after entry the patient suffered from two bouts of epistaxis. Examination revealed a bleeding point in the left nares, which was controlled by cauterization and packing. On the fiftieth hospital day she suddenly developed massive edema of the left arm and became markedly dyspneic. Edema of the legs increased in amount, and she died on the fifty-third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WALTER BAUER: "The small vessels removed showed acute thrombophlebitis." Was that a real thrombophlebitis?

DR. TRACY B. MALLORY: It might be furier to say "acute thrombosis"—a fresh thrombus with no inflammatory reaction whatever.

DR. BAUER: A real thrombosis?

DR. MALLORY: Yes.

DR. BAUER: I do not believe there can be much doubt but that this woman fell ill eight months prior to admission. The question is, Was the initial illness related to what was subsequently found in her chest? I think there can be little doubt that she was suffering from migratory phlebitis or phlebitis migrans. The story is quite characteristic of this disease syndrome. Whether migratory phlebitis is a distinct disease entity, no one really knows. It is a relatively rare condition. I suppose it is more frequently encountered in thromboangitis obliterans than in any other disease. It may be the first symptom of thromboangitis obliterans. Involvement of the superficial veins is quite characteristic. It begins peripherally, disappearing in one area only to reappear at another a little closer to the heart. This patient was a woman. We know that thromboangitis obliterans is a relatively rare disease in women. We have no other symptom suggesting its existence in this patient. With the premise of migratory phlebitis followed by a sudden attack of pain in the right chest one might reasonably conclude that this patient had what was diagnosed on the outside by a roentgenologist—a pulmonary infarct. However, I believe pulmonary infarction is rarely encountered in phlebitis migrans. This is due to the fact that the process starts externally

and as a rule involves the external and middle coats of the vein. Complete resolution usually occurs in one portion of the vein only to have the process begin elsewhere. Pulmonary infarction is so infrequent that those working in the Peripheral Vascular Clinic do not advocate ligation of the vein in order to prevent pulmonary infarction. I think there are exceptions to this rule. Dr. Mallory can set me straight on this.

DR. MALLORY: My experience is limited, but the cases other than Buerger's disease on which I have seen a biopsy have shown thrombosis regularly, inflammatory reaction in the vessel walls rarely.

DR. BAUER: The literature on this disease is very meager. The only place I looked it up was in Homans's textbook. Therein it states that in migratory phlebitis one rarely needs to worry regarding the possibility of pulmonary infarction because it occurs so rarely. This is due to the fact that the pathologic process proceeds from within.

DR. MALLORY: I think Dr. Homans believes that thrombosis can occur and spontaneously resolve very rarely.

DR. BAUER: That is obvious from the course of the disease. It may involve a vein in the region of the wrist or ankle with obvious signs and symptoms persisting for several weeks only to disappear completely. Later the same process may occur in the region of the elbow and subsequently higher up the arm. I think we have to be very cautious in interpreting these chest x-ray films. Ordinarily we should say that sudden pain in the chest occurring in a patient with phlebitis means pulmonary infarction. Infarction with infected emboli should cause tissue necrosis, cough and foul-smelling sputum. We are unable to state just what the situation was in this case. It is of interest that there was a two months' interval between the onset of the first venous thrombosis and the appearance of sudden severe pain in the chest. At this time there was no evidence of phlebitis. To have a pulmonary embolus at this late date would be unusual. The fact that this patient had no fever is another reason for wondering if the pleural pain was not due to some cause other than pulmonary infarction. This pain persisted from the very onset. You might argue that she had had an infected pulmonary infarct with subsequent abscess formation, lasting three and a half months. This would be unusual in the absence of fever. The fact that her temperature was only 99°F on entrance is significant. The sputum which she raised was always blood streaked. This is rather unusual, is it not, Dr. King, in the

case of pulmonary abscess or an infected pulmonary infarct

DR. DONALD S. KING Yes.

DR. BAUER This bit of evidence is helpful. She did have a leukocytosis running around 25,000. She developed enlarged suprahilar lymph nodes. One might argue that they were part and parcel of the phlebitis. However they persisted despite the fact that the phlebitis disappeared. I wish the description of these lymph nodes was more detailed. They were tender. Were they firm or hard? I should be inclined to believe that this woman was suffering from a migratory phlebitis but that in addition she had cancer of the lung. We shall have Dr. Hampton discuss the x-ray films in greater detail a little later. I should be inclined to believe she probably had metastatic carcinoma of the lung rather than a primary tumor. If she was suffering from metastatic carcinoma, where was the primary tumor? I believe that the supraclavicular nodes were sentinel nodes. I may be wrong because it is possible for inflamed lymph nodes to persist a long time. The continued blood streaking and absence of fever would fit pulmonary cancer better than pulmonary disease in consequence of repeated pulmonary infarction regardless of whether or not the emboli were infected. These metastatic lesions were bilateral. They may have been secondary to carcinoma of the breast or hypernephroma. Dr. Hampton can the metastases of hypernephroma be relatively diffuse?

DR. AUBREY O. HAMPTON They could be similar to those in this case.

DR. BAUER We know she had some red blood cells in the urine. If I were to guess I should say that her primary lesion was a hypernephroma and that she had metastases to the lungs. I think it is highly probable that this woman's exitus was due to a pulmonary infarct. I do not believe that repeated pulmonary infarction alone explains the entire situation. I shall say what I think before Dr. Hampton discusses the x-ray films. If I have reason to change my mind later I hope that I shall be allowed to do so.

I shall summarize by saying that this patient had a hypernephroma with bilateral metastases to the lungs, and migratory phlebitis. She probably died because of a pulmonary embolus. I doubt if she had the generalized form of pulmonary osteoarthropathy, for no generalized bone pain was present, she did however have the localized form.

DR. F. DENNETTE ADAMS Do you attach any significance to the report of monilia in the sputum?

DR. BAUER I am happier leaving that finding

alone rather than trying to attach any significance to it.

DR. KING On the wards the therapeutic attack was on the basis of the infection with monilia and large amounts of iodide were given.

DR. BAUER That is all right by me, but I should prefer to leave the monilia alone because I think it is a red herring. I may be wrong because I do not know anything about yeast infections of the lung.

DR. HAMPTON I am sure this chest picture changed in the time between the outside examination and this one. These quite sharply defined round areas in the left lung could not be infarcts. They are due either to metastatic abscesses or to metastatic carcinoma. The shadow that was interpreted as infarct does look somewhat like one, if you believe infarcts are triangular in shape.

DR. MALLORY How about a septic infarct?

DR. HAMPTON Septic infarcts or metastatic abscesses could produce this picture. This triangular shape appears at the base of the upper lobe—the middle lobe is not involved particularly no more than any other part of the lung; however, the lesion looks more like one due to collapse of a portion of the upper lobe than to an infarct. I cannot say positively that it is not an infarct, but it is more like collapse. Certainly if it is an infarct it has been there long enough to reduce the lung in size and to become very sharp in all directions and more like a triangle than an infarct should be. Over a period of months we have evidence of increase in size of this area of density thus indicating a progressive disease without pleural fluid, and in this spot film you see a very definite round mass. I do not know which side this mass occupies, but I assume it is in this area here at the right. She did have swelling of the soft tissues around the terminal phalanges without bone changes.

DR. BAUER Could such an x-ray picture be secondary to a primary cancer of the lung?

DR. HAMPTON Yes.

DR. BAUER Would you be inclined to think that this lesion here plus the other findings, was consistent with metastatic carcinoma?

DR. HAMPTON I could not explain the triangle on the basis of cancer but I could account for the round mass on the basis of metastasis.

DR. BAUER Is it fair to ask Dr. Hampton to make a diagnosis?

DR. MALLORY Yes at this stage.

DR. BAUER I do not believe I shall change mine.

DR. HAMPTON I should explain the small focus at the base of the right upper lobe as being due to a primary tumor. It could however, be due to metastatic infection or to metastatic malignancy.

DR BAUER Let us leave for a moment the question as to whether it is primary in the lung or elsewhere. If we make a diagnosis of malignancy are you willing to make in addition a diagnosis of pulmonary infarction?

DR HAMPTON No

DR BAUER What would be the easiest way to explain the exitus?

DR HAMPTON That triangular lesion could be an infarct. We did not have a film taken after death, which would show the infarct if it happened at that time.

DR BAUER I shall leave it that way. I was not able to interpret whether this was primary carcinoma of the lung or the result of metastases.

DR MALLORY There is one other piece of information which was withheld. I do not believe it would have helped you much. One of the lymph nodes in the neck was biopsied and showed an unclassified malignant tumor, probably a carcinoma.

DR KING What do you think about the recurrent hemoptysis in relation to whether it was primary or metastatic cancer of the lungs?

DR BAUER It would fit primary carcinoma of the lung much better. If I had given that more thought, even though I did not have the expert interpretation of the x-ray films, I should have come nearer to making what I now believe is the right diagnosis, namely primary carcinoma of the lung.

DR J. H. MEANS I should like to speak on one point. I did not have this patient in charge but saw her once on teaching rounds. I agree entirely with Dr. Bauer's thought that she had a migratory phlebitis. He raised the question whether you can get embolism in this disease. I shall merely cite a patient of mine who I think had the same disease. He did have a series of pulmonary emboli with infarcts but without any infection, as in this case. These cleared up rapidly. After he had had his tonsils out and had his epidermophytosis cleared up he recovered. Whether that had any relation to the migratory phlebitis, I do not know, but Dr. Arthur W. Allen who saw him in consultation expressed the belief that a fungous infection might play a role in the etiology of migratory phlebitis. I mention the case because of the embolism. I am sure it may occur.

DR BAUER Yes, but as I have said it is so rare that litigation is not indicated.

There is one other point about thromboangitis obliterans. At the Mayo Clinic they have tried to prove that it is an infectious disease. The evidence thus far is not very convincing.

CLINICAL DIAGNOSES

Carcinomatosis
Phlebitis migrans

DR BAUER'S DIAGNOSES

Carcinoma of the lung (? primary, ? metastatic),
with widespread pulmonary metastases
Phlebitis migrans
Pulmonary infarct
Pulmonary osteoarthropathy

ANATOMICAL DIAGNOSES

Primary carcinoma of the lung, right middle lobe, with extension and metastases to opposite lung, mediastinum, pericardium, pleura and lymph nodes
Thrombophlebitis of femoral and common iliac veins and inferior vena cava
Hydrothorax
Hydropericardium
Leiomyomas of the uterus
Atherosclerosis of the aorta and coronaries, minimal

PATHOLOGICAL DISCUSSION

DR MALLORY So far as the migratory phlebitis of Buerger's disease is concerned, in the acute stage it regularly shows a highly specific picture with multiple milium lesions made up of monocytes and giant cells that suggest milium tubercles or gummas. This patient did not show any such picture. I think that is an important point against Buerger's disease as the cause of the phlebitis in this case.

The autopsy showed that the primary lesion was in the middle lobe of the right lung. It was a nodule of cancer about 5 cm in diameter, surrounding and growing into the primary bronchus of the right middle lobe. There were multiple metastases throughout both lungs, the result of extension both through lymphatics and the blood stream. Metastasis had occurred to other parts of the body. Many of the retroperitoneal nodes were involved, as well as those that you have heard about in the neck. The phlebitis was very extensive and involved a great many large veins as well as small ones. In fact both femorals, both iliacs and the inferior vena cava itself for a distance of 8 cm were filled with thrombus. Why an embolus had not broken off I cannot imagine, but there was not a single infarct in the lungs.

DR BAUER You have not explained the sudden exitus.

DR MALLORY No. A possible thing was that she had a carcinomatous pericarditis with a significant amount of fluid—300 cc.

Dr. BAUER Cardiac tamponade?

Dr. MALLORY Perhaps Three hundred cubic centimeters of fluid would not produce tamponade in a normal pericardial sac but with the walls stiffened and rendered inelastic by cancer it might.

Dr. BAUER I should think the mistake I made was in not interpreting the continuous blood streaking correctly I should have realized that that would be rather unusual with metastatic carcinoma.

Dr. KING We have seen a few cases about three or four, where hemoptysis has occurred with metastatic malignancy.

Dr. HAMPTON That discussion came up some time ago We looked it up after a fashion and as we reviewed the cases that were treated in the Tumor Clinic we found that metastatic carcinoma very rarely produces hemoptysis.

Dr. BAUER That is very significant If I had interpreted it properly I should have made the correct diagnosis the first time Such points are extremely important to remember

CASE 25432

PRESENTATION OF CASE

A thirty-eight year-old woman was admitted to the hospital from a tuberculosis sanatorium complaining of malaise.

The patient had been in a weakened and run-down condition for ten or fifteen years, with poor resistance to respiratory infections and an inability to gain weight. She had suffered repeated attacks of severe "colds" and had seven severe attacks of quinsy during the past eighteen years. The most recent and severe peritonsillar abscess occurred two and a half years before admission and required two separate incisions, with drainage of large amounts of foul-tasting pus. On all occasions the abscesses were incised without anesthesia and she recalled having aspirated none of the draining purulent material. The patient stated that the tonsils were partially removed in infancy but that she had not been able subsequently to have a complete removal. Much of the patient's life had been spent in England, Australia and Canada. She was fairly well until sixteen months before admission when she contracted a severe "chest cold and bronchitis" similar to many other attacks she had experienced in the past. She had the usual course of a cold for a few days after which there remained a persistent hard cough which was productive of not more than a teaspoonful of yellow non foul sputum. There were no other symptoms save weakness and easy fatigability. X-ray films were taken which confirmed the clinical diagnosis of pulmonary tuber-

culosis. The x ray findings were reported as showing infiltration of the right lower lobe, and a small mass seen in the right hilus region was interpreted as being an enlarged lymph node. The sputum was positive for tuberculosis. About fourteen months before admission she entered a sanatorium where bed rest and supportive measures were instituted. She improved rapidly both subjectively and objectively so that she gained weight, felt renewed vigor and noted a subsidence of cough, although she raised about a teaspoonful of sputum a day for several months. For the first three months of sanatorium care the sputum was positive for tubercle bacilli, but since then the monthly sputum examinations had been negative. X-ray films were reported to show good improvement of the parenchymatous infiltration, but the mass in the region of the right hilus was observed to increase in size, with cavity formation. During the recent months before entry she had almost no cough except for a few days following each of three bronchoscopic examinations. Approximately one month before admission she awakened from an afternoon nap and found her mouth full of a large quantity of foul-tasting purulent material intermixed with blood. The taste resembled that of the material obtained from incision of her peritonsillar abscesses in the past. She was referred to this hospital for further study.

The physical examination showed a well developed well-nourished, healthy looking woman in no distress. There was slight dullness posteriorly with diminished breath sounds and increased tactile fremitus and spoken and whispered voice from the fifth rib downward on the right. The remainder of the examination was negative. The temperature, pulse and respirations were normal. Blood and urine examinations were negative. The corrected blood sedimentation rate was 0.15 mm per minute. Chest fluid injected into guinea pigs before hospital admission was found to be negative for tubercle bacilli. The blood Hinton test was negative. X-ray films of the chest revealed an oval mass at the apex of the right lower lobe in contact with the sixth and seventh dorsal vertebrae and extending from the sixth rib to the eighth interspace. The mass was 6.5 cm in length and 4.5 cm in width. An irregular cavity with a fluid level was present within the mass. The walls of this cavity were a little over 1 cm in thickness. The periphery of the mass was smooth. There was definite thickening of the pleura overlying the vertebrae presenting somewhat the appearance of an abscess around these vertebrae but the vertebral bodies were normal and the joint spaces were preserved. The heart and mediastinum were slightly dis-

placed to the right, but there was no mediastinal shift with respiration. The left lung was clear. The right lung was also clear except for the area described and two small irregular areas, one at the apex and one at the base of the upper lobe. The diaphragm moved well.

On the eighth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR ALFRED O. LUDWIG: In this case we are faced with the necessity of explaining the nature of what appears to be an abscess. I do not believe we can get around the diagnosis of tuberculosis because it is very clear she had a positive sputum examination on many occasions. I wonder if Dr. Hampton will show the x-ray films first. There is no mention of plates of the cervical spine, I wonder if any were taken.

DR AUBREY O. HAMPTON: This patient brought some films with her. The most striking thing is, of course, this sharply defined oval mass in the apex of the right lower lobe which was described in the report. The mass had gradually increased in size over a period of several months, eventually breaking down in the middle, and now shows a very irregular thick-walled cavity. There was also a small round mass at the base of the right upper lobe, which, during the period the large one increased in size, diminished and almost disappeared. The spine does not show anything abnormal. There was an attempt at connecting this lesion in the lung with the pleura, but this was not successful.

DR LUDWIG: There was nothing in the examination of the dorsal spine that allowed you to think there might be tuberculosis of the vertebrae?

DR HAMPTON: No, I was interested in demonstrating whether or not the pleura was adherent. If it were adherent you might get more evidence that it was an inflammatory lesion, but of course such a finding would not be sufficient to make a diagnosis.

DR LUDWIG: I think, first of all, that this woman had pulmonary tuberculosis, but I do not believe it is possible to correlate the presence of pulmonary tuberculosis with this mass. The latter must represent some different process. The first thing I thought of is a possibility, which I dismiss, was that this woman might have had tuberculosis of the dorsal or cervical spine with formation of a paravertebral abscess. I have never heard of such an abscess's occurring in this position. We have seen them appear in the region of the psoas muscle subsequent to cervical and dorsal vertebral lesions, so they can do strange things, but in the absence of positive x-ray findings anywhere in the

spine I do not believe we have the evidence to make such a diagnosis. This woman did have peritonsillar abscesses but I do not believe we can relate these to the presence of tuberculosis. I can not imagine that a peritonsillar abscess would heal as well as this one did, if it were of tuberculous origin. I should think it possible that this woman may have had a lung abscess secondary to peritonsillar abscess, but there are several things about such a diagnosis that are difficult to correlate with what we are given. In the first place the whole course is a strange one for a pulmonary abscess of the ordinary sort. She did have foul sputum, but so far as I can tell she never had much in the way of a febrile reaction. We are not told anything about leukocytosis, I think we have to assume it was absent.

DR TRACY B. MALLORY: There was none or two counts that were done at this hospital. I do not know about the sanatorium findings.

DR LUDWIG: Furthermore, the blood sedimentation rate was 0.15 mm per minute, a normal figure, and this is another point against an active septic process.

I am confused about the description given of the chest findings and shall ask Dr. King to help. "Slight dullness posteriorly with diminished breath sounds and increased tactile fremitus and spoken and whispered voice." To my mind the chest findings do not fit together. I should think if the patient had had partial collapse of the lung on the right there would have been diminished instead of increased tactile fremitus. If the bronchi were open I should think the breath sounds would have been increased rather than diminished.

DR DONALD S. KING: You cannot put much emphasis on these signs.

DR LUDWIG: I imagine that the patient may have had partial collapse. Was there any x-ray evidence of that, or of partial bronchial obstruction?

DR HAMPTON: No. All we see is a mass occupying the apex of the right lower lobe. If it were primary in the bronchus, the latter would be so small that it would not produce any picture of collapse.

DR LUDWIG: There was slight displacement of the heart and mediastinum to the right, but there was no mediastinal shift with respiration.

DR HAMPTON: The mass is not in the region of the right main bronchus, and the slight displacement of the heart might be blamed partly on scoliosis, which she had, and partly on scarring of the right upper lobe from old tuberculosis.

DR LUDWIG: We have no evidence of pleural effusion, except that chest fluid was injected into

a guinea pig. She might have had an effusion previously.

DR. KING: The physical signs could be signs of a mass with some compression of the lung.

DR. LUDWIG: The diagnosis of pulmonary abscess of the ordinary sort is a very unsatisfactory one. I believe. She did bring up some blood at one time.

DR. MALLORY: One point worth considering is that there was no objective evidence as to foul sputum. We have only her word for it.

DR. KING: She brought that out clearly herself. She was certain it was foul sputum and noted the same sort of taste she had experienced when the peritonsillar abscesses broke.

DR. LUDWIG: This woman probably had a pulmonary abscess which suddenly drained at that time. It would be interesting to know what the febrile course was before and after the time she awoke and found the foul sputum in her mouth. She was probably afebrile because the abscess was relatively well drained for the time being. I wonder if the cavity could have been due to tuberculosis with secondary infection. It is nothing like the ordinary tuberculous cavity and with the disappearance of the other lesion I do not believe we can hold to that point of view.

How about tumor? So far as I am concerned it could be possible. I should like to ask Dr. Hampton about that.

DR. HAMPTON: That was the great argument. Because of the thick wall, the sharp peripheral outline and the broken-down irregular center the lesion grossly suggests tumor more than anything else, but there was a round nodule in the base of the right upper lobe which disappeared.

DR. LUDWIG: Is there any possibility that this lesion was of the type that we have seen in sarcoid at the hilus?

DR. HAMPTON: No.

DR. LUDWIG: Is it not true that they never break down?

DR. HAMPTON: Yes.

DR. LUDWIG: If there were lymphoma there is no evidence elsewhere in the body and again I do not believe lymphoma breaks down.

DR. HAMPTON: Rarely.

DR. LUDWIG: I shall make the diagnoses of pulmonary tuberculosis and pulmonary abscess which was probably metastatic from a peritonsillar abscess and which had increased in size and then drained. The reason we have so little evidence of inflammation and activity is that the abscess had drained. Pulmonary abscesses may be caused either by aspiration or by septic pulmonary emboli from the region of infected tonsils or elsewhere. Dr. King, can you tell us what the present feeling is about that?

DR. KING: It depends on whose opinion it is. In this hospital we believe that the aspiration theory explains the great majority of cases.

DR. HAMPTON: If the patient had a chronic lung abscess, would not the wall of the abscess be thin?

DR. LUDWIG: I should think it would be thick.

DR. KING: The more chronic the abscess the thinner the wall. Is that right, Dr. Mallory?

DR. MALLORY: I am not sure. By a ray that might seem to be the case as the surrounding area of consolidation cleared up. I do not believe we have ever seen an abscess wall as thick as this one was.

DR. LUDWIG: That knocks the props out from under my diagnosis. If it is a tumor, it is a strangely behaving one. I shall stick to my original diagnosis.

DR. MALLORY: The films on this case have been around the country and a great variety of diagnoses have been made. The field is open if any one would like to make further suggestions.

A PHYSICIAN: How about hydatid cyst? She had been in Australia.

DR. HAMPTON: A hydatid cyst has a very thin wall.

DR. ALLEN G. BRAILEY: Is not two and a half years from the last peritonsillar abscess something of an objection to a diagnosis of lung abscess?

DR. MALLORY: Yes, that is a good point.

DR. KING: This case was presented to a board of experts at an "Information Please" contest which Dr. Holmes arranged for the National Tuberculosis Association. The diagnosis made there by the experts was the same as that which has been made by Dr. Ludwig, but if this performance had been conducted as the regular radio program it would have cost the sponsoring company ten dollars.

PREOPERATIVE DIAGNOSIS

Tuberculoma

DR. LUDWIG'S DIAGNOSES

Pulmonary tuberculosis
Pulmonary abscess

ANATOMICAL DIAGNOSIS

Tuberculoma of lung

PATHOLOGICAL DISCUSSION

DR. MALLORY: This lobe was resected by Dr. E. D. Churchill who in the course of the operation noticed several little nodules on the pleura which he believed were very suggestive of tuberculosis. When the lobe was finally removed and sectioned a very large caseous mass was found at the apex of the lobe, with four or five smaller scattered

lesions elsewhere. The lesion was almost completely filled with caseous material. The cavity did not appear so large in the specimen as it did in the x-ray plates, and the diagnosis is tuberculoma. It is a type of reaction to the tubercle bacillus that is not uncommon in other organs, but we do not often see it in the lung. The vast majority of such lesions break down and form a cavity.

DR KING: The nodular or circular lesions of pulmonary tuberculosis are recently receiving a good deal of attention because they are very easily confused with pulmonary tumors. There are reports in the surgical literature of cases operated on for carcinoma that have proved to be due to tuberculoma. Most of the circular lesions are smaller than the one in this case. Sometimes the round lesion is the end stage of a primary infection and remains healed, but in our experience at the Middlesex County Sanatorium these

lesions are very apt to develop a cavity in the center, giving a doughnut type of shadow in the x-ray, these doughnut-like lesions usually spread rapidly.

DR HAMPTON: I wish we had the other films. She had a small tuberculoma in the base of the right upper lobe that disappeared.

DR LUDWIG: Is it not somewhat unusual to have a tuberculous cavity appear in this situation?

DR HAMPTON: No.

DR LUDWIG: As close to the spine as this one?

DR HAMPTON: We used to think so, but since the chest surgeons have been collapsing cavities we have found quite a few.

DR LUDWIG: Was there any other organism in this tuberculoma?

DR MALLORY: We did not culture it. The slides, however, do not suggest any secondary infection.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

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THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

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SUBSCRIPTION TERMS: \$6.00 per year in advance, postage paid, for the United States; Canada, \$7.04 per year; \$8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Mass.

NEW ENGLAND

POSTGRADUATE ASSEMBLY

THE second New England Postgraduate Assembly will be held on Tuesday and Wednesday of next week at Sanders Theatre, Harvard University, Cambridge. Invitations have been sent to every registered physician in New England, and the applications for badges and tickets already received by the committee indicate that the attendance will be even greater than that in 1938, when approximately nine hundred physicians were registered. This year's meeting is officially sponsored by the Massachusetts, New Hampshire and Rhode Island and Vermont State Medical Societies and the Maine Medical Association.

Last year's program was received so enthusiastically that no change in the general scheme has been made by the Program Committee. Eleven carefully chosen guest speakers, all prominent edu-

cators as well as successful practitioners in their particular fields of medicine, will deliver twenty two thirty minute talks on subjects of practical and timely interest, there will be no discussions. Buffet luncheons will be served in Memorial Hall on both days, and will be followed by an address on Tuesday and a question period on Wednesday. The dinner on Tuesday evening, also served in Memorial Hall, will be followed by a talk by a member of the Federal Bureau of Investigation of the United States Department of Justice.

The registration fee (three dollars) does not include admission to the luncheons (fifty cents each) or the dinner (one dollar). Those desiring tickets for the latter should apply immediately, if they have not already done so to the Postgraduate Assembly Committee, 8 Fenway, as only a limited number of tickets will be available at the registration desk in the corridor of Memorial Hall. Such applications should be accompanied by a check or money order, and if they are received by the committee on the week of the assembly the applicant must claim his badge and tickets at the registration desk.

This is an unusual opportunity for all New England physicians to obtain the latest and best information in regard to the diagnosis and treatment of a variety of diseases, and it is hoped that but few will fail to make the most of it.

A NEW ORGANIZATION INTERESTED IN MEDICAL EDUCATION

IN the later years of the nineteenth century scientific contributions concerning the etiology of many diseases and the methods of dealing with them imposed on institutions engaged in educating physicians the responsibility of adjusting their methods to meet the demands of this revolution in medical practice. Some of the schools were progressive and adjusted their curricula to meet the situation. A considerable proportion however, were poorly equipped, inadequately endowed or carried on for the financial benefit of the controlling interests, and among these, conditions were intolerable in many instances.

The first effort designed to bring about the indicated reformation was the enactment of state registration laws designed to protect the public from incompetent practitioners and also to bring about better educational methods in medical schools. It was hoped that medical schools would adjust their methods to provide better prepared candidates for state approval. Unfortunately most of the proposed laws were so modified before enactment that the situation throughout this nation was far from ideal because of the lack of uniformity of important provisions relating to medical pedagogy and the admission to practice of the graduates of schools the curricula of which were based on theories that were at variance with scientific knowledge. Some states had several registration boards operating under different standards of medical education, thereby enabling irregulars to practice medicine.

In 1904 the American Medical Association came to appreciate the necessity of more effective action within the profession and created the Council on Medical Education and Hospitals, with the avowed object "to investigate conditions of medical education, hospitals and associated subjects and to suggest means and methods by which the same may be improved." The officers of the Council took up the imposed responsibilities with enthusiasm, collected facts and recommended the retirement from the field of medical education of more than half of the then existing schools. This was brought about and today there are seventy-six medical schools in the United States and Canada recognized by the Council. Furthermore, medical schools, hospitals, the Federation of State Medical Boards of the United States, medical societies and educational institutions having direct or associated functions covering medical education are co-operating with the Council. Although it has no authority to compel adoption of its recommendations or standards, the quality of its work has inspired respect for its decisions and brought about among the faculties of the approved educational bodies a disposition to adopt, so far as possible according to local conditions, the standards defined in the Council reports.

Even with the creditable advances made in the last thirty-five years the opinion is current that modern medical education is not a static or perfectly organized plan for training physicians, as shown by differences in methods and standards in the curricula of various schools. As this sentiment pervaded the minds of those particularly interested in the matter, it was expressed in conferences of groups and brought to the attention of the Annual Congress on Medical Education and Licensure in Chicago in 1938, with the recommendation that representatives of those bodies interested in medical education should unite for the purpose of study and concerted action in bringing about progress in this field. This proposition was severely criticized in an editorial in the February 26, 1938, issue of the *Journal of the American Medical Association*.

The plan, however, was not abandoned, and on June 24, 1939, delegates from organizations interested in medical education, met and created the Advisory Council on Medical Education. The names of the delegates present at this meeting are as follows: William S. Middleton, M.D., Wilford C. Rippley, M.D., and Maurice H. Rees, M.D., of the Association of American Medical Colleges; Robin C. Buerki, M.D., Rt. Rev. Msgr. Maurice F. Griffin and Christopher G. Parnell, M.D., of the American Hospital Association; Rev. Fr. Alphonse M. Schwitalla, S.J., of the Catholic Hospital Association; Walter L. Biering, M.D., Jesse W. Bowers, M.D., and the late Harold L. Rybins, M.D., of the Federation of State Medical Boards of the United States; Franklin G. Ebaugh, M.D., John Green, M.D. and Byrl R. Kirklin, M.D. of the Advisory Board for Medical Specialties; Arthur W. Allen, M.D., and Dallas B. Phemister, M.D., of the American College of Surgeons; Edwin B. Fred, Ph.D., and Clarence S. Yoakum, Ph.D., of the Association of American Universities; and Anton J. Carlson, Ph.D., of the Division of Medical Sciences, American Association for the Advancement of Science. The American College of Physicians, also a participating organization, had appointed J. Howard Means, M.D., and Hugh J. Morgan, M.D., as delegates, and the American

Public Health Association and the National Board of Medical Examiners had designated Walter S. Leathers, M.D., but neither was able to attend. Other organizations included, as voted at the meeting, are the Association of American Colleges and the American Protestant Hospital Association. The following officers were elected: Dr. Rappleye, president, Dr. Rees, vice-president, Dr. Buerki, secretary-treasurer.

The Council on Medical Education and Hospitals of the American Medical Association was invited to send delegates to this meeting, but since the Reference Committee on Resolutions of the House of Delegates of the Association had reported that this action was inadvisable, the invitation was not accepted, however, the committee submitted the recommendation that communications received from the new council should be given consideration. This action of the committee was construed by some as a wish to avoid an alliance which might not be advantageous to the official representatives of the American Medical Association, particularly in view of the fact that the Council on Medical Education and Hospitals of the American Medical Association had recommended the sending of delegates to the meeting.

Regardless of any interpretation of the purposes of the founders of this new organization, the constitution adopted by it should dispel suspicion of any antagonism to the American Medical Association or to the work of the latter's Council on Medical Education and Hospitals. The part relating to its proposed function reads as follows:

This council is created to meet the need of a central agency representing the universities, medical schools, hospitals, licensing bodies, specialty boards, public health agencies and other national organizations in this country which deal with different phases of medical education. The council shall serve as a clearing house for the co-operative consideration of those problems and programs of professional training with which more than one group is concerned, as a medium of consultation and mutual assistance in the formulation and support of adequate educational standards, and as an agency for advice and recommendations to member and other organizations dealing with medical education.

The study of this portion of the constitution and other information at hand warrants the belief that this council is not desirous of usurping the power and influence of any department of the American Medical Association. Its members regard the American Medical Association as the parent organization in this country and one which is entitled to the highest position in dealing with the problems relating to medical education. It is apparent that the council hopes to pattern its work on the general activities of the Medical Council of Great Britain. In general, the members realize that they have no executive power but hope to contribute advice as they see occasion for it and engage in the study of such problems as may be delegated to committees. At this meeting, committees were appointed to study conditions relating to interstate endorsement of medical licensure and the hospital intern problem.

With these facts before us and with knowledge of the standing of the men behind this movement to create another group interested in medical education, it is reasonable to suggest that any suspicion of unworthy motives should be held in abeyance until there seems to be a foundation for it. By their works we shall know them.

OBITUARY

SETH MARSHALL FITCHET

1887-1939

Seth Fichet was a robust individualist, a modest and sincere man, an able and sympathetic physician. He hated sham and pretense in others and he was never guilty of either himself. He enjoyed life, but he did not flinch when he knew that death for him was very near.

At the age of eighteen, justly believing that he had not received his proper reward at the hands of his teachers, he left school and enlisted as a seaman in the United States Navy, serving with the Pacific Fleet for four years. He was discharged with the rank of chief petty officer and as the injustice which had been meted out to him in school had by then been corrected he returned to finish his course. Failing any financial backing his academic pursuits were necessarily carried out entirely on his own resources with the help of occasional scholarships.

He entered the Harvard Medical School with the class of 1919, but as soon as the United States entered the World War, he enlisted and after a preliminary period of training at Plattsburg was commissioned a captain in Battery E of the 301st Field Artillery.

During his training at Plattsburg he sustained a severe injury when a camouflaged gun pit caved in, fracturing several cervical vertebrae and leaving him after a prolonged convalescence with a slight residual paralysis. It was characteristic of the man that minor incidents such as this could not be allowed to interfere with duty, and with no complaints or incriminations, he carried on, went with his battery to the French front and was cited for bravery in action at Verdun and at Chateau Thierry. When the war was over he returned home as major and maintained his commission in the Reserve Corps until 1934, finally resigning as a lieutenant colonel.

When mustered out of active military service, he returned to the pursuit of his studies at the Harvard Medical School and graduated with the class of 1921.

After a surgical internship at the Massachusetts General Hospital, he entered private practice, maintaining, however, staff appointments both at the Children's Hospital and the Massachusetts General Hospital. In 1938 he became surgical director and chief-of-staff of the Josiah B. Thomas Hospital in Peabody.

Seventeen months before his death, he consulted one of his closest medical friends for what seemed to be a minor ailment. It was apparent, however, that the malignant disease from which he actually was suffering was already far advanced and no possibility of cure existed. In spite of this, Seth Fitchet, the soldier, returned to his work and remained at his post as long as he could—courageous and simple and victorious to the end.

A. T. Jr.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

SEPTIC ABORTION

Mrs. J. J., a twenty-four-year-old para II, was admitted to the hospital August 1, 1910, stating that she was approximately ten weeks' pregnant.

A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

Her present illness began three weeks before admission with chills and fever, which had persisted up to entrance. For the past seven days there had been severe lower abdominal pain and, for twenty-four hours, vomiting. The patient emphatically denied any attempt to induce an abortion. In the light of subsequent findings the truth of her denial is open to grave doubt.

The family history was not obtained. The patient's past history was uneventful. She had had no serious illnesses or operations. There had been one full-term normal delivery, with normal pregnancy and puerperium, two years before. Catamenia had begun at thirteen, were regular with a twenty-eight-day cycle and lasted five days. She stated that her last period had begun on May 15.

Physical examination showed a well-developed and nourished woman with a flushed face. The tongue was coated but moist. The temperature was 100°F, the pulse 102 and of good quality. The heart sounds were regular, no murmurs were heard. The lungs showed uniform resonance. The abdomen was soft, but tender in both lower quadrants, with slight muscular spasm. On vaginal examination there was a good multiparous perineum, a soft cervix and some blood-tinged vaginal discharge. The uterus was symmetrically enlarged to a size corresponding to a three or four months' pregnancy, differing from the patient's history. The vaults were tender, but no masses were felt. The white-blood-cell count was 12,000, the hemoglobin 90 per cent. The urine was clear, with a specific gravity of 1.008, and showed a slightest possible trace of albumin and no sugar. The sediment contained many leukocytes, red blood cells and epithelial cells.

The temperature rose steadily to 103°F on the fourth day after admission, the pulse remaining between 100 and 110. The blood-tinged discharge continued. A diagnosis of septic threatened miscarriage was made, and it was deemed wise to empty the uterus. The cervix was dilated under ether anesthesia, and the cervical canal and lower uterine segment were tightly packed with sterile gauze. No apparent progress was made during the next twenty-four hours, so the pack was removed and another pack introduced without anesthesia. The patient quickly bled through the second pack. She was again etherized, and as she was bleeding freely, it was decided to complete the dilatation in order to empty the uterus. A fetus and placenta were extracted manually without injury to the cervix. No curet was used. The bleeding ceased when the uterus was emptied, and the patient was returned to bed in good condition.

The temperature, which had dropped to normal

just before delivery, rose again the following day to 102°F., and after a few days of elevation gradually fell to normal on about the fourteenth postpartum day.

The patient was discharged on the eighteenth postpartum day in good condition. The os was closed, there was a bilateral laceration of the cervix, the uterus was well involuted and in good position, and the vaults were clear.

Comment. This case well illustrates the conservative method of handling a threatened septic abortion. The continued rise in temperature and the small amount of bloody discharge were evidence that the contents of the uterus were infected. The size of the uterus—between three and four months—was definite evidence that the patient's story could not be relied on.

It is important in such cases that the uterus be emptied as gently as possible. Packing of the cervix and lower segment of the uterus for the purpose of softening the cervix and initiating labor is much safer than any attempt at instrumental dilatation and emptying the uterus at one sitting. It is quite possible in this case that had the second pack been left, in spite of the hemorrhage, labor would have started within the next twenty-four hours and the uterus emptied itself spontaneously. The hemorrhage which followed the second gauze packing was unquestionably initiated by the separation of some of the placenta. The rise in temperature to 102°F. on the day following the emptying of the uterus was definite evidence that infection existed. Strict conservatism was followed, no douches being administered in the course of the next week, the temperature gradually came down to normal and the patient was discharged relieved on the eighteenth day.

Had an attempt been made to dilate manually this three and a half month uterus and empty it, tremendous hemorrhage would have resulted requiring transfusion. Furthermore, the injury to the uterine wall which accompanies such a maneuver would undoubtedly have spread the infection. The uterus is very tenacious of its contents from three and a half to six months, if it has to be emptied the more conservative the method chosen, the safer the operation.

MEDICAL POSTGRADUATE EXTENSION COURSES

This week marks the beginning of the Fall Session of the Medical Postgraduate Extension Courses, given by the Massachusetts Medical Society in co-operation with the Massachusetts De-

partment of Public Health, the United States Public Health Service and the Federal Children's Bureau. Programs have been arranged in nine of the eighteen districts of the Massachusetts Medical Society, and printed schedules have been mailed to all physicians in these districts.

The courses include the following general subjects: cardiovascular disease, gonorrhea, syphilis, obstetrics, pediatrics, pneumonia, oculo-urology, and head and spine injuries. However, the district programs have been made out according to the selections of the local committees. The eight or ten meetings in each district will be held at a specified time and place which have been so picked that they should be convenient for the majority.

* * *

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning October 30.

BARNSTABLE

Sunday November 5 at 4:00 p.m., at the Cape Cod Hospital Hyannis. Cardiovascular Disease. Eleven important questions about heart disease and their answers. Instructor Ashton Graybiel. Donald E. Higgins, *Chairman*.

BRISTOL NORTH

Thursday November 2, at 4:00 p.m., at the Morton Hospital Taunton. Cardiovascular Disease. Eleven important questions about heart disease and their answers. Instructor R. Earle Glendy. Lester E. Butler, *Chairman*.

BRISTOL SOUTH (New Bedford Section)

Friday November 3, at 4:00 p.m., at St. Luke's Hospital New Bedford. Common Problems of Neurology. Indications for lumbar puncture. Instructor T. J. C. von Storch. Robert H. Goodwin, *Chairman*.

ESSEX NORTH

Friday November 3, at 4:30 p.m., at the Lawrence General Hospital Lawrence. Syphilis in Pregnancy and the Offspring. Instructor Rudolph Jacoby. John Parr, *Chairman*.

*ESSEX SOUTH

*MIDDLESEX EAST

MIDDLESEX NORTH

Friday November 3 at 4:45 p.m., at St. John's Hospital Lowell. Pneumonia. Instructor Maxwell Finland. William S. Lawler, *Chairman*.

*WORCESTER DISTRICT (Milford Section)

WORCESTER DISTRICT (Worcester Section)

Friday November 3, at 8:00 p.m., in the Staff Room of the Worcester City Hospital Worcester.

The course will be omitted October 31 because of the New England Postgraduate Assembly.

Gonorrhea in the Female. Instructor Oscar F Cox, Jr George C Tully, *Chairman*

Worcester North

Friday, November 3, at 4 30 p.m., in the Nurses' Home of the Burbank Hospital, Fitchburg Complications in Obstetrics, Illustrated by Case Histories Instructor John Rock. George P Keavney, *Chairman*

DEATH

SCANLAN—THOMAS J SCANLAN, M.D., of West Roxbury, died October 18. He was in his sixty-eighth year.

Born in Oregon, he attended Tufts College Medical School, receiving his degree in 1903. During the World War, he served as a captain in the medical corps, having previously assisted the late Dr Eliot Wadsworth in Red Cross work. At the time of his death Dr Scanlan was chairman of the Board of Trustees of the Boston State Hospital. He had served as a member of the staff of the Boston Dispensary, consulting surgeon at Deer Island Hospital, medical examiner for the City of Boston law department, member of the gynecological staff of St. Elizabeth's Hospital, chief consultant at the Foxboro State Hospital and surgeon at the Winthrop Community Hospital.

Dr Scanlan was a fellow of the Massachusetts Medical Society and American Medical Association and a member of the New England Obstetrical and Gynecological Society.

His widow, a sister and two brothers survive him.

EXPRESSIONS OF APPRECIATION

The following expressions have been passed by the Senior Staff of the Boston City Hospital in appreciation of Mr Joseph P Manning and Dr George G Sears, who have recently resigned from the Board of Trustees.

WILLIAM P BOARDMAN, M.D., *President*,
Senior Staff, Boston City Hospital

* * *

JOSEPH P MANNING

For twenty-eight years a trustee of the Boston City Hospital appointed trustee on April 28, 1911, resigned on May 1, 1939. For twenty-one years chairman of the Board of Trustees. On April 1, 1927, the trustees assumed management of the Boston Sanatorium, when this institution came under the jurisdiction of the Boston City Hospital as the Sanatorium Division.

The professional staff of the hospital wishes to acknowledge its appreciation of his contributions to the management and development of the institution during these years. Under his wise guidance it has grown from a collection of small two-story buildings to the present excellently serviceable, modern hospital. His honest and prudent disposition of large expenditures of millions of dollars has never been questioned by the taxpayers or by responsible city officials. His care and supervision in building and maintenance have shown a complete mastery of hospital administration. His patience and dignity, often in trying circumstances, eloquently preclude any criticism.

Lastly, may we attest to his high and understanding co-operation with the members of the professional staff,

a dignified, courteous and fair hearing was always accorded them. The present renown and standing of the hospital is his monument.

It is our earnest wish that he may be with us for many years to enjoy the reward of a life fruitfully spent in the service of his fellow man.

GEORGE G SEARS

Physician to the Boston City Hospital, active and consultant, for forty-six years, trustee for twenty-one years. A gentle and lovable physician, a distinguished teacher, a wise administrator. Recognized and honored by degrees from Amherst and Harvard for contributions to the medical world. A gentleman learned and scholarly, a large part of whose busy life was diligently devoted to the hospital he loved.

Appointed outpatient physician in 1893, he served faithfully through all the grades of the staff from the lowest to the highest. Returning as trustee in 1918 he gave to the hospital the benefit of his long years of close association with the institution. His thorough knowledge of the professional problems of the hospital brought a fine balance to the Board of Trustees and was of invaluable aid to the solution of its difficulties.

The professional staff of the hospital hereby records its sincere appreciation of his learning, his devotion and his long years of zealous service to the institution in whose growth from a small, undeveloped unit to its present enviable position he has had such a vital part. With grateful hearts, they salute him and wish him many years of health and happiness.

MISCELLANY

MAINE NEWS

RAGWEED SURVEY

Two pollen stations were operated for the 1939 ragweed survey, one at Portland on the roof of the Maine General Hospital and under the supervision of the hospital superintendent and the other at Camden under the auspices of the Camden Chamber of Commerce. These stations were opened August 10 and were continued for fifty days.

BOARD OF REGISTRATION OF MEDICINE

Physicians licensed to practice medicine and surgery in Maine on July 12, 1939, are as follows:

THROUGH EXAMINATION

William Champlin Burrage, Portland
Harry Edward Christensen, Portland
Joseph Francis Dinan, Boston
John Francis Dougherty, Bath
Edward Thomas Driscoll, Worcester, Massachusetts
Lucio Ernest Gatto, Cambridge, Massachusetts
Harold Floyd Gilbert, Mt. Holly, New Jersey
Napoleon Gingras, Augusta
Marlin Charles Moore, Kulpmont, Pennsylvania
Arthur Ames Nichols, Boston
John Coleman Nunemaker, Boston
Richard Rapp Owens, MacMahan Island
Maurice Swain Philbrick, Skowhegan
George Emil Ronne, Pawtucket, Rhode Island
Robert Somerville Borden, Bristol, New Brunswick, Canada
Douglas Willey Walker, Thomaston
Lester Ray Whitaker, Portsmouth, New Hampshire
Russell Wigh, Boston
Frederick F Yonkman, Boston

THROUGH RECIPROCITY

Frederick Scarborough Gray Portsmouth New Hampshire
 Allen Harold Knapp, Calais
 Stanley Walter Machaj Portsmouth New Hampshire
 James Calvin Martin, Baltimore
 James Mitchell Parker Chestnut Hill Massachusetts
 Arthur Gilson Pilch Bloomfield, New Jersey
 George Capron Poore, Philadelphia
 Irvin Robert Schaen, Cincinnati

PREMEDICAL EDUCATION AT MIDDLESEX UNIVERSITY APPROVED

In response to the request of Middlesex University for approval of its Junior College for giving premedical education, the Approving Authority has given provisional approval for the school year 1939-1940 and has so notified the institution. The decision was made after inspection of the buildings, facilities and equipment, interviews with members of the faculty and an examination of the financial statements submitted. With the notification of approval the Authority made certain recommendations, which it is reported the trustees are taking steps to carry into effect.

Under an act of 1936 amended in 1938 creating the Approving Authority no candidate matriculating in a medical school after January 1, 1941 will be admitted to the examination for registration as a qualified physician if he has not had, before entering medical school two years of premedical education in a college approved by the Approving Authority.

OTE

The promotion of Dr. LeRoy A. Schall instructor in laryngology at the Harvard Medical School to the position of Walter Augustus Lecompte Professor of Otolaryngology and Professor of Laryngology as of September 1, 1939 as recently announced at Harvard University. He succeeds Dr. Harris P. Mosher who has become professor emeritus. Dr. Schall graduated from Jefferson Medical College in 1917. He has been on the staff of the Harvard Medical School since 1926 and on the staff of the Massachusetts Eye and Ear Infirmary since 1923 serving as surgeon in otolaryngology since 1935. He has also been assistant surgeon in laryngology at the Palmer Memorial Hospital since 1932.

CORRESPONDENCE

BIOGRAPHY OF DR. HARVEY CUSHING

To the Editor: Mrs. Cushing has requested me to prepare a biography of her husband and I should be most grateful to anyone who wishes to make letters, anecdotes or other memorabilia available.

Copies of all letters no matter how brief are desired, and if dates are omitted it is hoped that when possible, these may be supplied (for example, from the postmark). If original letters or other documents are submitted they will be copied and returned promptly.

A new medical library building is being erected at the Yale University School of Medicine to receive Dr. Cushing's library and collections including his letters, diaries and manuscripts. Any of his friends who wish now or later to present correspondence, photographs or other

memorabilia for permanent preservation among the Cushing papers will receive the appreciative thanks of the University.

JOHN F. FULTON, M.D.

333 Cedar Street,
 New Haven Connecticut.

THE MULTIPLE EPIDERMAL PUNCTURE TEST

To the Editor: I should like to call to the attention of your readers a skin-testing technic that I have been using for several years—the multiple epidermal puncture test. It is performed by placing the allergen on the skin and making about twelve microscopic punctures through the material directly into the epidermis. The test substance should cover an area about 3 mm in diameter. The needle used for the punctures should be a solid one, as a perforated needle will obviously lead to test contamination.

The multiple epidermal puncture test is a simple one and once mastered can be performed rapidly. It gives uniform results and is very sensitive. Since the punctures are microscopic, trauma and bleeding are not produced and tell-tale test marks are not left on the skin. The test is not painful and for this reason is particularly useful in testing children. Furthermore, a large number of tests can be performed at one sitting.

ANGELO L. MAIETTA, M.D.

408 Main Street,
 Winchester Mass.

ERRATUM

In the paper "The Reciprocal Pharmacologic Effects of Amphetamine (Benzedrine) Sulfate and the Barbiturates," by Dr. Abraham Myerson which was published in the October 12 issue of the *Journal* the sentence beginning the fourth paragraph on page 561 should read

It is a synergist to atropine in all the physiologic effects of that drug* or conversely atropine is a synergist to amphetamine sulfate because it blocks or inhibits the action of the parasympathetic nerves and allows the sympathetic effects of amphetamine sulfate to be more firmly established.

In editing the copy a transposition was made so that the sentence as published, implies that amphetamine sulfate acts on the parasympathetic nervous system. Ed.

NOTICES

BOSTON GASTROENTEROLOGICAL SOCIETY

The next meeting of the Boston Gastroenterological Society will be held in the Dowling Amphitheater of the Boston City Hospital on Wednesday November 8, at 12 o'clock noon.

Dr. Howard M. Clute will deliver an illustrated lecture on "Cancer of the Stomach."

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic of the Peter Bent Brigham Hospital will be held on Wednesday afternoon November 1 at 2:00. Drs. Elliott C. Cutler and Soma Weiss will speak on "Cough, Chest Pain." A clinicopathological conference, conducted by Dr. Elliott C. Cutler will follow.

On Thursday morning, November 2, at 8 30, there will be at the Peter Bent Brigham Hospital a combined clinic, conducted by Dr Soma Weiss, of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital

Physicians and students are cordially invited to attend

ELLIOTT C CUTLER, M.D., *Secretary*

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday evening, November 7, at 8 15

Dr Morris Fishbein, editor of the *Journal of the American Medical Association*, will speak on "American Medicine and the National Government."

DAVID B STEARNS, M.D., *Secretary*

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide, former concertmaster with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, every

Thursday at 8 30 p.m., in Studio A, Station WMEX, 70 Brookline Avenue, Boston Those interested in becoming members should communicate with Dr Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430)

FAULKNER HOSPITAL

The usual clinicopathological conference of the Faulkner Hospital will be held at the Faulkner Hospital on Thursday, November 2, at 5 00 p.m. There will be a discussion of cases by Drs W R. Ohler and E L. Young, Jr

All interested members of the medical profession are cordially invited to attend

BOSTON INFECTIOUS DISEASE SOCIETY

The Boston Infectious Disease Society will meet in the Laboratory Study of the Children's Hospital on Thursday, November 2, at 4 30 p.m.

PROGRAM

Panleukopenia of Cats A virus disease. Dr W Hammon

Observations in the Role of Birds and Mosquitoes in the Spread of Equine Encephalomyelitis Dr W A Davis

Experiments with *Haemophilus influenzae* (human) in Swine Dr John Mote

LEROY D FOTHERGILL, M.D., *Secretary*

AMERICAN SANATORIUM ASSOCIATION

The sixteenth fall meeting of the Eastern Section of the American Sanatorium Association will be held at the Westfield State Sanatorium, Westfield, on November 3 and 4 Scientific sessions will be held on Friday afternoon and Saturday morning, and Friday evening there will be

an x-ray conference in charge of Dr F Maurice McPherson, of the Germantown Hospital, Philadelphia

WILLIAM HARVEY SOCIETY

A meeting of the William Harvey Society of Tufts College Medical School will be held in the auditorium of the Beth Israel Hospital, Boston, on Friday, November 4, at 8 00 p.m. Dr Shields Warren will speak on "The Effect of Radium and X-ray Irradiation on Tissues" The meeting will be conducted by Dr H E MacMahon

On Friday, December 8, Dr Richard H Overholt will address the society on the topic "Clinical Studies in Primary Carcinoma of the Lung" Dr James Hepburn will act as chairman

Members of the medical profession and their friends are cordially invited to attend

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Haverhill	November 1	William T Green
Lowell	November 3	Albert H Brewster
Salem	November 6	Harold C Bean
Brockton	November 9	George W Van Gorder
Gardner	November 14	Mark H Rogers
Northampton	November 15	Garry deN Hough, Jr
Worcester	November 17	John W O'Meara
Pittsfield	November 20	Francis A Slowick
Fall River	November 27	Eugene A McCarthy
Hyannis	November 28	Paul L Norton

AMERICAN ACADEMY OF DERMATOLOGY

About 600 leading dermatologists from all parts of the nation are expected to attend the second annual meeting of the American Academy of Dermatology and Syphilology at the Bellevue-Stratford Hotel, Philadelphia, November 6 to 8 inclusive. Sessions will be held in the form of symposiums, special lectures in "courses" lasting from one to four hours each, and numerous luncheon round table discussions

There will be over fifty lecturers on the three-day program including the guest speaker, Dr Cornelius P Rhoads of the Rockefeller Institute, New York City, who will speak at 11 a.m., Monday, November 6, on "Vitamin Complex" Among those on the program are Drs John G Downing and Jacob H Swartz, of Boston, whose respective subjects are "Eczema (all forms)" and "The Treatment of Resistant Mycotic Infections with Ethyl Iodide Inhalations Clinical presentations will take place at Jefferson Medical School, Philadelphia, all day Tuesday and November 7

Registration begins at 5 p.m., Sunday, November 5, followed by meetings of the Membership Committee and the Board of Directors The first executive session is at 10 a.m., Monday, and in the evening, following special lectures and a luncheon round table discussion there will be a dinner meeting of the Board of Directors and a smoker The annual banquet is set for 7 p.m., Tuesday Four symposiums, concerning syphilis, allergic pharmaceutical therapeutics, and the physiology and chemistry of the skin, are to be held Wednesday morning, November 8

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY OCTOBER 30

MONDAY OCTOBER 30

8:15 p.m. New England Heart Association Boston Medical Library
8 Fenway Boston.

TUESDAY OCTOBER 31

9-10 a.m. "Measles" Professor Edwin B. Wilson, Joseph H. Pratt
Diagnostic Hospital

10 a.m.-12:30 p.m. Boston Dispensary tumor clinic.

WEDNESDAY NOVEMBER 1

12 m. Clinicopathological conference Children's Hospital Amphitheater

2 p.m. Joint medical and surgical clinic Peter Bent Brigham Hospital.

THURSDAY NOVEMBER 2

8:30 a.m. Combined clinic of the medical, surgical, orthopedic, and
pediatric services of the Children's Hospital and the Peter Bent
Brigham Hospital (the Peter Bent Brigham Hospital)

4:30 p.m. Boston Infectious Disease Society Laboratory Study of
the Children's Hospital

5 p.m. Faulkner Hospital clinicopathological conference.

FRIDAY NOVEMBER 3

10 a.m.-12:30 p.m. Boston Dispensary tumor II c.

12 m. Clinical meeting of the Children's Medical Service, Massachusetts
General Hospital, Eder Doane.

12 m. Urological conference at the Massachusetts General Hospital
lower amphitheater Out-Patient Department.

8 p.m. William Harvey Society Auditorium of the Beth Israel Hos-
pital

SATURDAY NOVEMBER 4

10 a.m.-12 m. Medical staff rounds of the Peter Bent Brigham Hos-
pital. Conducted by Dr. Soma Weiss.

*Open to the medical profession.

OCTOBER 27—Massachusetts Medical Society Page 633 issue of
October 19

OCTOBER 30—New England Heart Association. Page 587 issue of Octo-
ber 19

OCTOBER 31—Massachusetts General Hospital. Research meeting Page
631, issue of October 19

NOVEMBER 1—Peter Bent Brigham Hospital Joint medical and surgical
clinic. Page 628

NOVEMBER 2—Combined clinic of the medical, surgical, orthopedic and
pediatric services of the Children's Hospital and the Peter Bent Brigham
Hospital. Page 676

NOVEMBER 2—Boston Infectious Disease Society Page 676.

NOVEMBER 3—Faulkner Hospital, clinicopathological conference. Page
676.

NOVEMBER 3—William Harvey Society Page 676.

NOVEMBER 3-4—American Sanatorium Association Page 676.

NOVEMBER 6-8—American Academy of Dermatology Page 676.

NOVEMBER 6-11—New England Medical Center Teaching Clinics on
Cancer Page 633 issue of October 19

NOVEMBER 7—Greater Boston Medical Society Page 676.

NOVEMBER 8—Boston Gastroenterological Society Page 675

NOVEMBER 8-9—New England Society of Physical Medicine in conjunc-
tion with the Academy of Physical Medicine, Hotel Kenmore, Boston.

NOVEMBER 9—Pennsylvania Association of Physicians. 8:30 p.m. Hotel
Barclay, Haverhill

DECEMBER 2—America Board of Obstetrics and Gynecology Page 1019
issue of June 15

DECEMBER 8—William Harvey Society Page 676.

DECEMBER 6, 1940—American Board of Obstetrics and Gynecology
Page 1019, issue of July 27

JANUARY 22-25, 1940—American Academy of Orthopaedic Surgeons.
Hotel Statler, Boston.

MARCH 7-9, 1940—The New England Hospital Association Hotel Statler
Boston.

MAY 14, 1940—Pharmacological Convention. Page 874 issue of May 25

JUNE 7-9, 1940—America Board of Obstetrics and Gynecology Page
1019 issue of June 15

DISTRICT MEDICAL SOCIETY

SUFFOLK

NOVEMBER 2—Censor meeting. Page 441 issue of September 14

NOVEMBER 29—Scientific meeting Treatment of Syphilis Dr. Harold T.
Hyma, Dr. Low Chargin, and Dr. William Leifer (New York City)

JANUARY 31, 1940—Scientific meeting. Subject to be announced later

MARCH 27—Scientific meeting Symposium on Ulcerative Colitis and
Diarrhea Under the direction of Dr. Chester M. Jones.

APRIL 24—Annual meeting in conjunction with the Boston Medical
Library Election of officers. Program and speakers to be announced later

BOOKS RECEIVED FOR REVIEW

Sketches in Psychosomatic Medicine Nervous and Men-
tal Disease Monograph. No. 65 Smith E. Jelliffe. 155 pp
New York Nervous and Mental Disease Publishing Com-
pany 1939 \$3.00

The Neurogenic Bladder Frederick C. McLellan. 206
pp Springfield, Illinois, and Baltimore Charles C
Thomas 1939 \$4.00

Circulatory Diseases of the Extremities John Homans.
330 pp New York The Macmillan Co 1939 \$4.50

Synopsis of Pediatrics John Zahorsky and T. S. Zahor-
sky Third edition. 430 pp. St. Louis C. V. Mosby
Co., 1939 \$4.00

A Synopsis of Surgical Anatomy Alexander L. McGreg-
or Fourth edition. 664 pp. Baltimore William Wood
& Co., 1939 \$6.00.

*Handbook of Bacteriology For students and practition-
ers of medicine* Joseph W. Bigger Fifth edition. 466
pp Baltimore William Wood & Co., 1939 \$4.25

*Pictorial Midwifery. An atlas of midwifery for pupil
midwives* Comyns Berkeley Third edition 166 pp
Baltimore. William Wood & Co., 1939 \$3.00

*Treatment of Some Common Diseases Medical and
surgical* By various authors. Edited by T. Rowland Hill.
398 pp Baltimore William Wood & Co., 1939 \$5.00

*The Dysenteric Disorders The diagnosis and treatment
of dysentery, sprue, colitis and other diarrhoeas in general
practice* Philip Manson-Bahr 613 pp Baltimore Wil-
ham Wood & Co., 1939 \$8.00.

Physiological Chemistry A text book for students Al-
bert P. Matheua. Sixth edition. 1488 pp. Baltimore
William Wood & Co., 1939 \$8.00

Cæsarean Section Lower segment operation C. McIn-
tosh Marshall. 230 pp. Baltimore William Wood & Co.,
1939 \$6.50

*A History of Tropical Medicine Based on the Fitz-
patrick lectures* H. Harold Scott. 2 vol. 1165 pp Bal-
timore William Wood & Co. 1939 \$12.50 per set.

Stedman's Practical Medical Dictionary Thomas L.
Stedman and Stanley T. Garber Fourteenth revised edi-
tion. 1303 pp. Baltimore William Wood & Co., 1939
\$7.50

Obstetrical Practice Alfred C. Beck. Second edition.
858 pp. Baltimore Williams & Wilkins Co., 1939 \$7.00.

BOOK REVIEWS

Doctors Nurses and Dickens Robert D. Neely 153 pp.
Boston The Christopher Publishing House, 1939
\$1.50

This is one of the most entertaining and delightful
books that has come into the reviewer's hands. The author
has selected those passages from Dickens's books which
treat of medicine, the doctor and his variety of assistants
such as nurses, interns, students and finally undertakers.
It was necessary to include them all in order to get a com-
plete picture. Furthermore, the title is sufficiently indefi-
nite to permit considerable rambling on the part of the
author. It is not only a pleasant intermezzo of medi-
cine as studied by Dickens in relation to all strata of so-
ciety but a delightful picture of Dickens's own life
troubles and vicissitudes. To one who reads the book it
will give not only a most pleasant and warm evening but

considerable food for thought. For instance, the sayings of Esther Summerson, the heroine of *Bleak House*, after her marriage to Dr Allan Woodcourt, show in what high regard Dickens held the medical profession. She says "I never walk out with my husband, but I hear the people bless him. I never go into a house of any degree, but I hear his praises, or see them in grateful eyes. I never lie down at night, but I know that in the course of that day he has alleviated pain, and soothed some fellow-creature in the time of need. I know that from the beds of those who were past recovery, thanks have often, often gone up in the last hour, for his patient ministrations. Is not this to be rich?"

It must be remembered that Dickens did satirize human life, but he did not do so to degrade it. He did not wish to pull down what was high into the neighborhood of what was low. He really satirized only the selfish and the hard-hearted and the cruel, he expressed in hideous light the principle which when acted on gives a power to man in the lowest grades to carry on a more terrific tyranny than if placed on thrones. The physician who gave of the milk of human kindness was treated with respect. On the other hand, he ridiculed the physician who with scientific outlook neglected his patient or those who gave lengthy scientific reports leading to nowhere. This is best shown by Dickens's characterization of the Mudfog Medical Association held in the town of Mudfog.

The carefully written text produced such an enthusiasm in the reviewer that he cannot help but recommend it to all and sundry.

Cancer Handbook of the Tumor Clinic, Stanford University School of Medicine. Edited by Eric Liljencrantz. 114 pp. Stanford University Press, 1939. \$3.00.

This handbook is based on postgraduate instruction in the diagnosis and treatment of malignant tumors given at Stanford University School of Medicine. It is in brief syllabus form and attempts to cover only the more frequent forms of the disease. Several useful diagrams are presented.

The diagram on page 3 regarding intrinsic and extrinsic factors in etiology might well be omitted. On page 5 an interesting family tree is presented showing three generations with a high incidence of carcinoma, particularly carcinoma of the breast. The reviewer questions the accuracy of bilateral breast cancers occurring as frequently as the diagram would imply, since involvement in the second breast is usually the result of metastasis or extension from that first involved rather than true primary bilateral tumor.

The brief chapter on "Principles of Radiation Therapy" is simple and straightforward. Cancers of the skin, eye and lip, of the oropharynx and neck, of the gastrointestinal tract, of the lung and of the breast are treated in brief chapters as are gynecological and genitourinary cancers, the leukemias and lymphoblastomas, tumors of the central nervous system and bone tumors. A brief bibliography is appended that deals primarily with recently published work. There are several excellent photographs of lesions of the skin.

In the treatment of cancer of the breast, operation is recommended in Stage I, and preoperative radiation or radiation without operation in Stage II. In Stage III roentgen castration is mentioned as an adjunct to treatment in cases in which cancer has occurred before the menopause.

In the discussion of carcinoma of the cervix a combination of radium and x-ray therapy is recommended in all except Stage I, where radium alone is advised.

The section on genitourinary cancer consists of five brief subdivisions, no one of which is sufficiently amplified to present any information of value.

This handbook would be of definite value for the third or fourth year student desiring a brief compendium of the important types of cancer, but falls short of giving sufficient information to be of value to the practitioner whose experience with malignant disease has been limited.

Syphilis, Gonorrhea and the Public Health. Nels A. Nelson and Gladys L. Crain. 359 pp. New York: The Macmillan Co., 1938. \$3.00.

The point of view of the authors of this book is definitely that of the public health officer, and it is written in simple straightforward language so as to be useful to the physician, social worker, nurse and such lay persons as are interested in the public-health aspects of the problem.

The first part of the book gives general information about genitoinfectious diseases and their incidence, prevalence, distribution and mortality. The rest of the book takes up control measures, costs, social hygiene considerations and what has been accomplished in Scandinavian countries.

The absurdity of many of the laws is humorously and effectively discussed, and the futility of merely "passing a law about it" is well shown. The authors recommend simple and flexible laws, which merely provide a background for sensible control measures. They add that it is useless to try to legislate good medicine without first providing good training for those who should carry out the treatment of the patients and the necessary control measures and that the laws should not control the physicians and health officers but be designed to be tools in their hands in order to be most effective.

Throughout the book the note is frequently sounded of helpfulness to the practitioner. That so much emphasis should be placed on this point is not surprising, since those who know Dr. Nelson and his work realize that he has always conspicuously conducted his department along this line. Any physician who fears interference from his state board of health should read the book with care, for the advisability of help and service to the practitioner is constantly reiterated.

Treatment in General Medicine. Edited by Hobart Reimann. 3 vol. 2834 pp. Desk index, 107 pp. Philadelphia: F. A. Davis Co., 1939. \$30.00.

This three-volume system on treatment in general medicine should prove valuable to the general practitioner. It is a complete source of information on all therapeutic procedures that come up in practice. In addition to the general topics considered in the average textbook on treatment, this work emphasizes psychotherapy and physiotherapy in their manifold applications, including occupational therapy and irradiation. There are also sections on minor surgical, gynecological and obstetric treatment, and on the care of the aged and of patients with cancer.

The work is a collaboration by thirty-four eminent American physicians, each an expert in his field. The volumes are well illustrated and substantially bound, and the print is excellent. There is a thorough index.

The New England Journal of Medicine

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VOLUME 221

NOVEMBER 2, 1939

NUMBER 18

THE CARE OF THE PATIENT*

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IT IS indeed an honor to be invited by the Faculty of the Harvard Medical School to address the student body on some phase of the care of the patient—a very great honor, in fact, when one considers that this has been an annual event for the past twelve years and that some very outstanding men in medicine have been invited to deliver this lecture. It is also a satisfaction to be able to discuss the care of the patient rather than his treatment, for it implies that one is interested in the patient's welfare as well as in his disease.

I wish to congratulate you on the wisdom you have displayed in choosing the Harvard Medical School in which to study, for this school holds a very enviable position among the fine schools of this country. In fact, Embree, in his review in 1935 for the Rosenthal Fund of America's great universities, placed Harvard first among the five foremost universities. And to be in Old Boston, which offers so much that is cultural and inspiring, with its fine medical tradition built over the years by outstanding clinicians and surgeons who have worked and taught in this time-honored institution, is an advantage.

In spite of the great advances in medicine in the last twenty years and the contributions which our profession has made in disease prevention, disease control and the prolongation of life, it is distressing to be told—and I have been informed on good authority—that about 13 per cent of the population, or nearly 15,000,000 persons, have been weaned away from the medical profession. Among them, unfortunately are the educated who have become faddists, those who have embraced Christian Science or faith healing and those who belong to the antivivisectionists and antivaccinationists. This last group however are often on the fence in their sympathies with our efforts as a profession. Then comes a group of less intelligent people who employ the cults—the

osteopaths, chiropractors and naturopaths, and below this group in the matter of intelligence are the patent medicine addicts, the victims of the quacks and a group of non-thinking persons who are just against doctors anyway. It will be difficult to reduce materially the numbers of the above-mentioned groups, but I firmly believe that by better treatment or better care or by education thus, in some measure, can be accomplished.

There is another group, however, who are not sympathetic with our work or our efforts because of disappointment suffered at our hands: those who cannot understand that certain diseases can not be cured, those who have been disappointed over the outcome of certain forms of treatment or operations, those who have been hurt and wounded by too much science and too little art, as modern medicine, unfortunately, is sometimes practiced today. This includes also a large number of people who break down today in merely trying to exist in our complex modern world and who are considered too often in a scientific light when what they need most of all is understanding and help with distressing problems in life which are often the true underlying cause of their ill health. This is an ever-enlarging group of people and it is most important that the modern physician become skilled in their management.

It is about this last mentioned group that I wish to speak for I believe that if our technic in approaching and treating these people could be improved, we could salvage great numbers of them and retain their sympathetic understanding of our efforts in their behalf instead of having them give themselves into the hands of the cultists and other charlatans.

It would be wrong of course to advocate less science in the teaching of modern medicine, it would be iconoclastic to advise that less interest be placed on problems of research or that there be less emphasis on the teaching of the specialties for we know too little about so much and there are still great discoveries and advances which

Lecture on "The Care of the Patient" presented at the Harvard Medical School, February 9, 1939.

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must be made, and which will continue to be made yearly. But I wonder oftentimes whether the student's training in the art of medicine is not being minimized, or at times neglected, because the science of medicine has become so intriguing and so fascinating—and the time is so short in which to review it all.

Here at Harvard you are fortunate in having professors who fully appreciate this situation, for here the true art of medicine is practiced and preached, and they feel so keenly about its importance that they have instituted these yearly lectures on the care of the patient.

I should like to review with you some of the influences which might be termed controllable and which keep large groups of people out of sympathy with our efforts for their welfare. In modern hospital and clinic work it is becoming increasingly more difficult to practice the art of medicine. The busy routine of an institution does not lend itself readily to a painstaking and broad consideration of the patient as an individual as well as of his disease. It is time-consuming to listen to a long story about home situations which at the time seem irrelevant, but often it is during the recitation of such homely things that the true cause of the illness under discussion is discovered.

It is in the busy life of a large institution that the young doctor may unconsciously acquire habits which will militate against his future success. The hurried, businesslike, serious approach to the patient—the thorough, systematic, orderly, quick but frigid first examination of some frightened, diffident patient—may give that patient an unfortunate impression of the institution and of its doctors. I was once an assistant of a famous surgeon who said he never wanted, as an assistant, a man trained in a near-by large city hospital, for while these men had had excellent training, there was a brusqueness, a roughness and a callousness about them that was very unfortunate. As he expressed it, the first encounter between the patient and the young doctor was “down with the bedclothes and up with the night-shirt” and a prompt and a fixed interest on the patient's diseased gall bladder rather than an interest in the patient who was unfortunate enough to have a diseased gall bladder.

I remember attending lectures in a city after I had finished my medical course, and of hearing the clinical professor of medicine, in a loud, booming voice, admonish his students with this caution: “Remember that the first duty of the physician is to search for and find the underlying pathologic process”—which he invariably tried to do with some quivering, terror-stricken patient shown before the class. This man was a great teacher,

but I was informed that he had an extremely difficult time in making a living. As a true scientist there was no one better, but he represented a type seen often, one who has much learning but very little wisdom.

In regard to the initial approach to our patients it is well to remember that they are all frightened, all apprehensive and many of them hypersensitive. It behooves every young man to develop a finesse in dealing with these people. It takes a certain personality to succeed in any walk of life. Many have it by natural inheritance, and others may acquire it by studying the ways of successful men and by developing within themselves those characteristics which make life a success, but, unfortunately, a few never can acquire the right type of personality which is so essential to success.

The student, the intern and every young physician should study the ways of his teachers, for invariably the successful teacher is a man of broad understanding and vision, a kindly man who is gentle and considerate with all his patients irrespective of their walks in life. I am grateful to my chiefs for teaching me many things which could not be learned in the operating rooms and in the laboratories, and I value my association with them while on rounds in the wards, in ward classes and in their consultation rooms, for there they dealt with human beings and not with unconscious patients or with laboratory problems.

As I have mentioned, functional disease is widespread and is increasing at a rapid rate. The present economic situation with its insecurity of the future is more than many of the population can withstand. We must remember that nearly all our patients having organic disease are mentally disturbed at the time of the first examination, and because of this it is of very great importance; but it is the patient who is functionally ill and with some organic lesion who demands a nicety of judgment to decide whether it is wise or best to concentrate our efforts alone on the organic lesion, to advise operation for the lesion or to treat the patient in a broad, general way, if there is no danger in delay. Many patients are accepted for operation in good faith and are thought to be well after the wound has healed per primam. They are listed as cured and return home to the troubled environment which may have been largely responsible for the illness. They then present a problem to the family physician and often to a psychiatrist, who may have reason to doubt the efficacy of the cure.

The anxious mother who is harassed by worries about her children or her husband and who has a retroverted uterus should not be accepted for operation without carefully weighing all sides of

the evidence, the young man with a duodenal ulcer whose symptoms are all exaggerated by an increase of emotional strain had better be treated by any method other than operation. On the medical service the head of a family with a heart lesion, whose nights are veritable nightmares because of economic situations and hardships which will arise should his job be lost because of his lesion, needs understanding of his problems as well as digitalis, the mother who is crushed with grief over the death of a child had better not be accepted for operation without a most careful consideration of just how much effect her grief may have on her health. These are just a few of the problems which we see almost daily in our work, but each illustrates the importance of considering the patient as an individual as well as his disease. Ill advised medical or surgical treatment of these patients is almost sure to be fraught with disappointment to the patient and to the doctor, and is one of the causes of having groups of people lose sympathy with our efforts.

The work of your great Cannon proves the harmful effect of emotions on bodily physiology. Would that its importance were more generally understood by our profession! The disastrous effect of fear is not fully appreciated. Long continued anxiety, apprehension, doubt and fear will undermine the nervous equilibrium of even normal, healthy people.

The offspring of wild animals at birth are without fear, but that instinct needs only a few days of mother training to be developed to a high degree. Unhappy is the lot of any wild thing which loses its mother during the first few days of life, for without the fear instinct developed it soon falls an easy prey to its many enemies.

Fear, therefore, as a means of protection has been of untold advantage to all species in their development, especially to man who survived not only, perhaps because he was fit, but because he knew when to retire and live to fight another time.

This instinct of self preservation to flee from danger and to avoid painful contact coming down to man through the ages, calls forth immense emotional activity. The thought or memory of an escape from an attack may cause the greatest degree of emotional excitement, so also the apprehending of an oncoming encounter with foe—or surgeon—may produce the same state of mind and even though the individual remains passive during it, his exhaustion will be more complete and more profound than if he had given vent to his emotions in some form of motor activity. It is a well known fact that fear associated with pain may exhaust the organism to the point of

death. Our surgical patients whose minds are racked with these emotions of fear and worry are often exhausted before they are anesthetized, and are fit subjects for surgical shock. In no other disease is the relation between fear and the severity and aggravation of symptoms better shown than in exophthalmic goiter. The reduction in the operative mortality in the treatment of this disease has not been due alone to improvements in technique. It has come about since we have gained a better understanding of the disease and of the harmful effects of fright on these patients. Crile's great work on anoci association is a monument to his splendid genius!

Cannon has shown that all bodily functions are altered and perverted by the emotions of pain, hunger, fear and rage—fear and rage being the most harmful. The preoperative rise in temperature, the fast pulse, the tremor, the insomnia and at times the glycosuria are the results of terror which grip the mind of the patient about to be operated on, oftentimes the subnormal temperature, the lost appetite, the drawn face and the languor seen in the postoperative patient are caused by grave worry and doubt. It is surprising to see the improvement in these patients as their mental attitudes are changed by suggestion.

Psychoanalysis reveals that much hysteria and psychoneurosis and many neurasthenic states have as their origin some past emotional upset—usually attended by fear or fright. We are all familiar with cases showing hysterical paralysis, aphonia, aphasia or blindness which can be definitely traced back to some terrifying emotion.

Granted, then that fear is a harmful emotion which may be the foundation of future mental illness that upsets bodily economy, retards convalescence, interrupts recoveries and when severe and associated with pain may cause death, is not an earnest effort on our part to eliminate this emotion from our patient's mind justifiable? What may we do in a practical way to eliminate it? In the first place, the patient should be considered from a psychological standpoint from the time he is admitted until after he leaves the institution. During his entire stay his mental welfare and comfort must receive the same careful consideration as does his physical welfare—for the majority of our patients are mentally as well as physically ill.

The personnel of the hospital should be chosen with great care, and the personality of each worker must suit the position he is to fill. Few of us realize how timid and diffident most of our patients are on admission or how easily they may be hurt by apparent inattention or frightened by

their new surroundings. It is so important to have their reception a cordial and a friendly one, for the first impressions they get of the hospital and of us are often lasting ones. And this is as equally true of the general practitioner's work in his office and in the home as it is of the hospital.

Great benefit may be had by the proper treatment of those who are ill from emotional causes. We all know the importance of a careful examination followed by the proper kind of suggestion. Many of these people, while not suspicious, are keen, and they are disarmed and lose confidence promptly if they sense any uncertainty in the mind of the physician as to the exact cause of their illness. For this reason I believe a discussion of the patient's case with associates in the presence of the patient is most unfortunate, especially should there be an uncertainty as to the correct diagnosis. The chiropractor or the quack never shows that he entertains the slightest doubt as to the correctness of his diagnosis, and what benefit his patients show comes entirely from suggestion.

In closing, let me emphasize another very important point in the care of the patient, that is, our patients should not be allowed to suffer unnecessarily during illness, after injury or after surgical operations, nor should they be hurt by painful dressings or manipulations which may be necessary. The apprehensive patient who is allowed to suffer without need cannot be convinced that his condition is satisfactory—it is far from being so to him and he fears an unsatisfactory or fatal outcome. It is important to use light gas anesthesia or short intravenous anesthesia for pain-

ful dressings, for *brisement forcé*, for certain cystoscopic examinations or for the removal of gauze drains. We are not handicapped as were the older surgeons, who, because there were no anesthetics except ether and chloroform, were obliged to hurt their patients, at times severely. These men were forced to excuse their acts by the statement, "I am hurting you now to help you later." The modern operator should not hurt his patients or allow them to suffer unnecessarily—the modern surgeon will not.

Broadly reviewing the question of the care of the patient as one who has spent his entire professional life in clinic and hospital practice, I believe that as physicians we cannot rely on our skill alone for our full measure of success, for it is necessary for us to give ourselves freely to our patients at all times. They need to be comforted, assured and bolstered up during illness and for the trying ordeals they may have to undergo. Our optimism must be constant, and we should be trained in practical psychology if our patients' minds are to be freed from the harmful emotions I have described.

Little touches of human kindness, strict and constant attention to the patient's mental welfare, will do much to rob our clinics and our hospitals of their cold, institutional atmosphere, which frightens so many of our diffident patients and interferes with many a satisfactory recovery—and equally important, such a plan will not only keep many of our patients loyal to our profession but will win back to our fold many who have deserted us for the cults.

THE EFFECT OF KITCHEN PROCEDURES ON THE VITAMIN C CONTENT OF FRUIT JUICES*

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IT IS the purpose of this paper to report the different effects of kitchen handling on the vitamin C content of the fruit juices in common use. The possibility of serious loss of vitamin C by naturally occurring oxidative processes during such manipulations was suggested by Daniel, Kennedy and Munsell,¹ who found a loss of about 10 per cent in the vitamin C potency of orange juice which had stood for six hours in a refrigerator. They further warned: "Since juices lose their scurvy preventing power on standing the common household routine of preparing juice in the evening for breakfast should not be practiced." This opinion has been circulated rather widely in both professional and lay channels.

We have studied the rapidity of oxidation of the vitamin at room temperature, in the icebox and in the double boiler. We have also mixed vitamin D-containing oils into orange juice to study whether they inactivate the ascorbic acid of the latter. Obviously the important clinical consideration is not so much the vitamin C content of the fresh juice as that of the prepared juice at the moment of consumption.

The quantity of ascorbic acid present in orange juice, tomato juice and pineapple juice, though subject to considerable variation, remains close enough to average figures for the clinician to utilize these substances with satisfactory approximation of prophylactic and curative doses. These doses have been determined with reasonable accuracy. Without entering here into a detailed discussion of the exact daily requirement one may summarize existing opinion²⁻⁴ by stating that the baby should have about 25 mg or more, and the adult 50 mg or more, of ascorbic acid daily. Moreover, it has been determined⁵⁻⁷ that a baby or adult suffering from scurvy can be saturated by the oral administration of about 200 mg of ascorbic acid given three times a day for three days, although much smaller quantities suffice to produce clinical improvement. That the baby's requirements are so close to those of the adult is doubtless due to the disproportionately large fraction utilized for growth processes.

For clinical purposes fresh orange juice, ac-

cording to Bessey,⁸ may be considered to contain 50 mg of ascorbic acid per 100 cc., provided the fruit has not been stored more than half a year. Bessey found no detectable loss of vitamin C in oranges stored for two months at 45 to 50°F., although losses of 10 to 35 per cent occurred after ten months. Likewise, canned tomato juice may be relied on to average 15 mg of ascorbic acid per 100 cc. McElroy and Munsell⁹ tested eleven brands and found them to vary between 8 and 26 mg per 100 cc., with an average of 17 mg. The average figure given for canned pineapple juice is 10 mg per 100 cc.⁸ Our own experience is in accord with these figures, as shown in Table 1.

However, the vitamin C content of a food at the time of consumption may be diminished from earlier values owing to naturally occurring oxidative processes. The time interval elapsing be-

TABLE 1 Ascorbic Acid Content of Canned Juices

TOMATO JUICE			PINEAPPLE JUICE		
S AMP NO.	ASCBIC ACID CONTENT mg per 100 cc		S AMP NO.	ASCBIC ACID CONTENT mg per 100 cc	
1	16.7		1	10.5	
2	12.7		2	9.6	
3	18.5		3	9.4	
4	17.7		4	6.4	
5	21.5		5	9.0	
6	21.4				
7	19.0				
8	18.0				
9	15.8				
10	15.4				
11	15.6				
12	15.6				
Average		17.0			9.0

fore consumption is thus of considerable importance. It has been also shown that ascorbic acid is very readily oxidized in alkaline solutions and is relatively stable in acids.¹⁰ Heating increases the rate of oxidation, as does the presence of copper which acts as a catalyst even in infinitesimal amounts.

Aside from the initial vitamin content of a food therefore, it becomes of importance to study the other conditions which may influence its final content. For instance, both cow's milk and woman's milk which have a very considerable content of vitamin C when fresh lose most of it following pasteurization and the delay consequent to marketing.^{11, 12} Obviously this is the reason why

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an antiscorbutic supplement has to be added to the infant's diet

When we come to examine the antiscorbutic juices in common use their protective acidity is noteworthy. The main variables are heat and time. It is not an uncommon routine for a housewife to squeeze the oranges the night before consumption, and it is her regular practice to open cans of tomato or pineapple juice for immediate consumption of part of the juice while the remainder is placed in the refrigerator for a few days. It is also not uncommon to find that the mother has been boiling the baby's orange juice as well as his formula, and the possible deleterious effect of this becomes of clinical importance.

The effects of heating and standing on the ascorbic acid content of orange, tomato and pineapple juices were investigated as follows. Fresh orange juice was squeezed into a tumbler, thoroughly mixed, filtered and divided into three

TABLE 2 *Effects of Time and Temperature on the Ascorbic Acid Content of Juices*

IN DOUBLE BOILER (95° C)		AT ROOM TEMPERATURE (27° C)		IN REFRIGERATOR (5° C)	
MIN UTES	ASCORBIC ACID CONTENT %	HOURS	ASCORBIC ACID CONTENT %	HOURS	ASCORBIC ACID CONTENT %
ORANGE JUICE (50.5 mg per 100 cc)					
0	100.0	0	100.0	0	100.0
20	91.0	3	96.0	4	100.0
50	88.1	5	92.1	24	93.0
70	88.1	21	90.1	70	72.1
95	87.1	28.5	86.1	94	53.4
115	85.1				
135	83.2				
TOMATO JUICE (12.1 mg per 100 cc)					
0	100.0	0	100.0	0	100.0
20	78.0	4	84.3	4	95.6
70	66.6	20	72.0	24	85.1
90	60.0	28	66.7	48	81.1
155	43.8			72	66.9
PINEAPPLE JUICE (7.2 mg per 100 cc)					
0	100.0	0	100.0	0	100.0
20	92.3	4	92.3	4	96.0
70	84.6	20	84.6	24	86.0
90	76.9	28	69.2	48	61.1
165	69.2			72	42.0

parts. One part was stored in a refrigerator, the second was left at room temperature and the third was kept in boiling water in a test tube tightly corked except for a small lumen. Loss of water by evaporation was practically negligible. Representative brands of pineapple juice and tomato juice were filtered and similarly divided. At suitable intervals aliquots were removed for titration with 2,6-dichlorindophenol. The results are shown in Table 2.

It is apparent, from a practical point of view, that little loss occurs when the juice is stored for a day in the icebox, or left in the kitchen for rea-

sonable lengths of time at room temperature. Although boiling very perceptibly increases the rate of oxidation, the fact that a housewife has brought the orange juice to a boil or even boiled it for three minutes is not sufficient grounds for regarding the juice to be worthless as an antiscorbutic. It still retains well over 80 per cent of its ascorbic acid after an hour at 95° C.

The effect of adding cod-liver oil or a concentrated antirachitic oil to an aliquot of 50 per cent orange juice is shown in Table 3. It is seen that

TABLE 3 *Effect of Adding Vitamin D Containing Oils on Stability of Ascorbic Acid in Orange Juice*

NO OF HOURS	TEMPERATURE	ASCORBIC ACID CONTENT		
		ORANGE JUICE CONTROL*	ORANGE JUICE PLUS OLEUM PERCOMORPH†	ORANGE JUICE PLUS COD LIVER OIL‡
		%	%	%
0		100.0	100.0	100.0
2	27° C	87.5	82.4	89.4
6	27° C	81.2	80.4	81.0
24	27° C	75.1	69.3	70.4
6	5° C	96.0	97.7	98.5
24	5° C	92.4	93.1	89.4
48	5° C	84.2	86.3	71.7

*Orange juice diluted with 50 per cent water (32.9 mg ascorbic acid per 100 cc)

†100 cc diluted orange juice plus 8 drops Oleum Percomorph

‡100 cc diluted orange juice plus 8 cc cod liver oil

no demonstrable catalytic effect is exerted on the oxidation of the vitamin.

COMMENT

Since the isolation and synthesis of ascorbic acid it has been shown that it is very readily oxidized in alkaline solutions and is relatively stable in acids. Heating tends to increase the rate of oxidation, as does copper acting as a catalyst. When oxidation proceeds at a slow rate, the time factor becomes of added importance.

Thus, although fresh cow's milk has a very appreciable ascorbic acid content, too much of the vitamin is oxidized during milking, pasteurization and marketing to make that food a reliable antiscorbutic agent. The breast-fed infant is amply protected since he contends neither with catalyst nor with time. It is apparent that it is not only the high vitamin content of citrus fruits but the protective acidity of the juice which makes them so efficacious as antiscorbutic foods, and it is no accident that these substances have become a routine part of the diet of the artificially fed infant.

Oxidation of ascorbic acid in orange, tomato and pineapple juices proceeds so slowly at icebox temperatures that the greater part of their vitamin C potency is retained after one or two days' refrigeration. The longer they stand, however, the greater is the destruction of the vitamin. Although the

rate of oxidation is materially increased at room temperatures, and greatly increased by boiling, it is not enough to necessitate particular caution in the ordinary kitchen handling and preparation of these juices

It seems justifiable for the clinician to assume that orange juice contains about 50 mg ascorbic acid per 100 cc., tomato juice 17 mg., and pine apple juice 10 mg. In his approximation of prophylactic doses he can consider 50 cc. of orange juice (containing 25 mg of ascorbic acid) as a nutritional unit, equivalent to 150 cc. of tomato juice or 250 cc of pineapple juice. The effect of usual home procedures can be ignored, although storage for more than two days, even in the icebox, has a progressively destructive effect on the vitamin

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CONGENITAL POSTERIOR URETHRAL VALVE CAUSING RENAL RICKETS*

Report of a Case

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ALTHOUGH many earlier observers¹⁻⁴ reported cases of late rickets associated with renal disease, Barber⁵ in 1921 was the first to designate "renal rickets" as a clinical entity. He defined it as "a condition of children marked by stunted development, often associated with bone deformities of the late rickets type and symptoms of a uremic character, due to severe renal insufficiency, frequently of congenital origin. The following case of renal rickets is reported because the etiologic obstructive lesion was demonstrated during life by proper methods of urethrography. This lesion is often overlooked unless visualization of the urethra is obtained.

CASE REPORT

A W., a 16-year-old, native boy entered the Beth Israel Hospital on June 30, 1937 with the complaint of knock knees of 1 year's duration. The family history was negative. The past history revealed his birth weight to have been 7 pounds. He was breast-fed during the first 3 months of his life. His first teeth appeared at 5 months. Bilateral undescended testes were noted by a physician at that time. At 14 to 15 months of age he stood up and at 18 months he walked. Bed wetting and dribbling of urine were first observed at the age of 3. The mother was told at that time that the patient suffered from pyelitis. Between the ages of 5 and 7 he had had pertussis, chickenpox and measles. Urinary incontinence was

present from the 3rd to the 10th year of his life, and up to 1936 he had nocturnal enuresis. Repeated urine examinations revealed pyuria. The mother noted the patient to be puny and of poor color. At the age of 11 after he had moved to a suburb, he developed asthmatic attacks in May and November and after 2 years these attacks occurred throughout the year. He did very good work in school and up to May 1936 had repeatedly received "A" in posture. At that time, knock knees, a duck-like gait and a left inguinal hernia were first noted.

On July 21 at another hospital left herniorrhaphy and left orchiopexy were performed. Two urine examinations revealed the specific gravity to be 1.004 and 1.010 with a very slight trace to a trace of albumin. The sediments showed abundant pus cells. On December 29, 1936, x-ray examinations were reported as follows: "The bones forming the shoulders show an increase in the amount of cartilage at the epiphyseal lines the bony trabeculations are unusually large and coarse. The same changes are present in all the bones. There is slipping of the epiphyses of both femoral heads." Further studies revealed persistent albuminuria, pyuria, loss of concentrating ability, normal blood pressure and a basal metabolism of -12 per cent. On discharge from that hospital on January 13, 1937 the diagnoses were: "Achondroplasia, hypothyroidism and hypoparathyroidism." Because of failure to improve, the patient came to the Beth Israel Hospital on June 30, 1937.

Examination on admission revealed an undersized alert boy with adenoid facies, sallow complexion and urinous breath. The height was 56 in., and the weight 74 lb. The skull was dolichocephalic. The skin was pallid yellow. The fundi were normal. The thyroid gland was symmetrically enlarged. The thoracic cage showed increased anteroposterior diameter, wide flaring of the costal margins and Harrison's groove. A rachitic rosary was palpated. The heart was not enlarged and presented normal rhythm, good quality of sounds and no murmurs.

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The blood pressure was 108/68. The lungs were clear. The abdomen was protuberant. Neither testis was palpated in the scrotum or inguinal canal. A marked degree of genu valgum was present without discomfort of the knees on motion (Fig 1). Enlargement of the wrists and ankles was noted. The armpits revealed numerous black hairs. The pubic region showed a good supply of

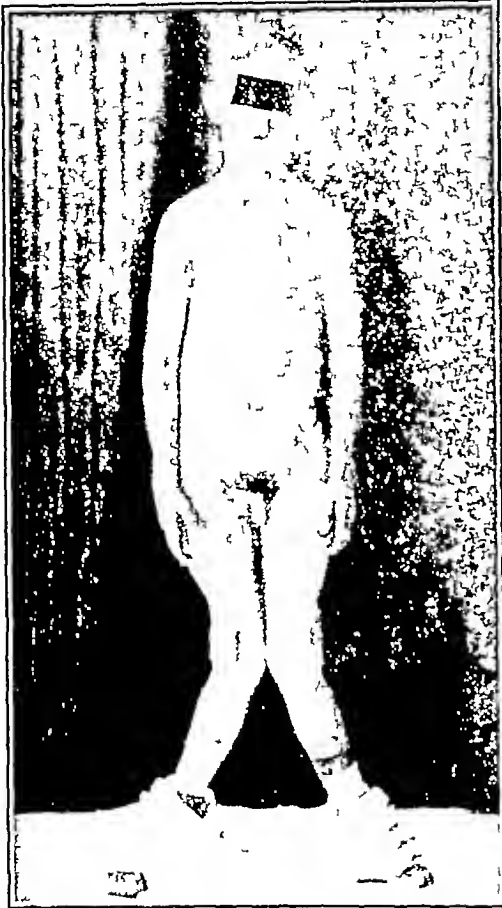


FIGURE 1 Photograph of the Patient Taken Nine Months before Death, Showing Genu Valgum

hair with a typical male distribution. The chin and cheeks showed a moderate amount of short, fuzzy hairs.

Numerous urine examinations showed a specific gravity ranging between 1.004 and 1.010, with a very slight trace to a trace of albumin in all specimens, centrifugal sediments revealed from 1 to 15 white blood cells and rare red blood cells per high power field. The red-blood-cell count ranged between 2,350,000 and 3,050,000, with a hemoglobin between 46 and 62 per cent (Sahli). The white-blood-cell count fluctuated between 6500 and 8200, two differential counts showed 16 and 2 per cent eosinophils and 61 and 65 per cent polymorphonuclears. Stool examination was negative for occult blood. Blood Hinton and Kahn reactions were negative. The blood sugar was 77 mg per 100 cc., the nonprotein nitrogen 111 to 126 mg, the creatinine 4.76 to 5.4 mg, the calcium 8.8 to 9.8 mg, and the phosphorus 5.9 to 7.0 mg, the total serum protein was 5.0 to 6.5 gm per 100 cc., the albumin 3.1 to 5.2 gm, and the globulin 1.3 to 1.4 gm, the blood carbon-dioxide combining power was 27 vol per cent. The serum phosphatase was 2.01 and 1.91 Kay units on two occasions.

The basal metabolic rate was +7 per cent. On two occasions after the intravenous injection of 6 mg of phenolsulfonephthalein, there was no excretion of the dye in 1 hour.

On x-ray examination the cranial bones were thin, ground glass in appearance and peppered with numerous small round areas of increased density. There was no evidence of increased intracranial pressure or other abnormalities. All the long bones exhibited a moderate degree of osteoporosis. The epiphyses were irregular and showed definite cupping, abnormal development and irregularities. The epiphyses of the upper ends of the humeri, ulnae, radius and femora were partially dislocated. There was an ovoid area of increased radiance in the upper portion of the shaft of the left tibia (Fig 2). The lower portions of the shafts of the right radius, left ulna and left radius were slightly bowed. The lower epiphyses of the middle phalanges, the lumbar vertebrae and the sacrum showed increased density. The lung fields were not remarkable. The anterior portions of the ribs were knobbed, widened and cupped. The ribs and scapulae showed slight decalcification.

Intravenous pyelography was not undertaken because of the presence of severe renal insufficiency. In order to rule out the presence of a congenital anomaly of the blad-



FIGURE 2 Roentgenogram Showing an Ovoid Area of Increased Radiance and Woolly Changes in the Metaphysis of the Tibia

der and urethra, a cystogram and urethrogram were taken on July 21, 1937. After 650 cc. of a 2.5 per cent solution of sodium iodide had been introduced into the bladder, the patient began to experience a sense of fullness. His bladder capacity was many times greater than normal for a 16-year-old boy. The cystogram showed the bladder to be markedly dilated, with pouching in its upper border and a slight depression of its base. The urethrogram revealed widening of the prostatic urethra. A filling defect in the upper left border of the dilatation

was consistent with a urethral valve of congenital origin (Fig 3)

As a result of the above findings, a suprapubic cystotomy for drainage was performed under local anesthesia on July 28 with the hope of subsequent surgical relief of the urethral obstruction. The bladder revealed a marked cystitis cystica. The trigone could not be outlined. The internal urethral orifice was atonic, leading to a dilated supracollicular prostatic urethra but it was impossible to determine whether there were valves distal to this cavity



FIGURE 3 Urethrogram and Cystogram during Voiding Showing Filling Defect in Prostatic Urethra and Bifurcation of Urethral Channel

On the posterior bladder wall there were two transverse ridges forming dilated pockets, the uppermost resembling a patent urachus. The ureteral orifices could not be visualized. A No. 34 Pezzar catheter was placed in the bladder and a Penrose drain was inserted in the prevesical space. Thereafter the case ran an uneventful course, the suprapubic wound healed gradually and the sutures were removed on August 1 and 2.

During the remaining month of his hospitalization the patient continued to be alert and symptomless. It is significant that following the institution of suprapubic drainage and a daily urinary excretion of about 3000 cc. there was no change in the kidney function (Table 1)

slight funneling in the region of the prostatic portico of the urethra

The patient was discharged on August 28. The diagnoses were Renal rickets, congenital urethral obstruction



FIGURE 4 Photograph Showing Small Contracted Kidneys Hydroureters Thickened Shrunken Bladder Ectopic Right Testis Attached to Right Ureter and Dilatation of Prostatic Urethra.

tion cystitis cystica cryptorchidism hydroureters and bronchial asthma.

He returned to the Outpatient Department of the Beth Israel Hospital on six occasions over a period of 7 months. The suprapubic catheter functioned properly and the patient did very well until smoky urine was noted for 2 days beginning January 24 1938. On January 26 a blood

TABLE 1 Representative Laboratory Findings

DATE	URINE FINDINGS				BLOOD CHEMICAL FINDINGS						
	SPECIFIC GRAVITY	ALBUMIN	CENTRIFUGED SEDIMENT		NON-PROTEIN NITROGEN	CHL. ATENON	PHOSPHORUS	CALCIUM	TOTAL PROTEIN	CARBON DIOXIDE COMBINING POWER	BLOOD PLEURAL
			White Blood Cells	Red Blood Cells	mg %	mg %	mg %	mg %	gm %	vol %	mm.
1937											
7/1	1.010	S T	6-12 (clumps)	Few	111	47	7.0	9.8	5.0	27.6	110/50
8/5	1.006	T	15-20	0	109	7.3	6.6	9.9	6.5	14.6	110/60
1938											
3/16	1.012	T	0-2	Many	143	6.3	6.4	6.7	6.7	42.4	128/70

On August 27 a cystogram was performed through the cystostomy tube. The bladder appeared considerably smaller as compared with that of the films of July 21. There was a moderate degree of reflux into the lower portion of the left ureter which appeared to be dilated. The base of the bladder was considerably thickened and there was

clot was passed through the cystostomy tube. On March 16 the patient reported that his urine had been grossly bloody for a week, that he suffered with weak spells characterized by rapid heart action and faintness and that he had experienced episodes of stiffening of his index fingers lasting from several minutes to 3 or 4 hours. Examina-

tion revealed pallor of the skin, uriferous breath, normal heart findings and absent Chvostek and Trousseau signs. Urine examination showed a grossly bloody urine. The blood nonprotein nitrogen was 143 mg per 100 cc. During the following month the patient became weaker, he lapsed into coma and died on April 28.

Autopsy Autopsy was performed by Dr. George White 12 hours after death. The kidneys were extremely small (Fig. 4), each measuring 7 by 3 by 2 cm. There were numerous adhesions between the kidney capsules and the renal beds. The capsules of the kidneys were irregularly thickened and markedly adherent to the underlying renal tissue and were stripped with great difficulty. The surfaces of both kidneys were studded with about a dozen thin-walled cysts varying from 1 to 2 cm in diameter. The contents of these cysts were clear and colorless. At the lower pole of the right kidney was a thick-walled cyst measuring 3 cm in diameter, the lining of which was smooth. There was no communication between the cyst and the pelvis of the kidney. Section of the kidneys revealed increased resistance, and the cut surfaces showed considerable distortion of the renal markings. The cortex was thinned and indistinctly demarcated. The medulla was irregular in outline. The calices and pelves were dilated, and the mucous membrane smooth. Microscopically, the renal tissue between the capsule and the pelvis was markedly reduced and was composed of scar tissue, few glomeruli and scattered tubules, many of which were dilated. Nests of small round cells were seen in the fibrosed areas. Many glomeruli showed varying degrees of fibrosis, increased cellularity and, rarely, adhesions between the capsules and the tufts. No crescents were seen. The cysts which were noted on gross examination were lined by a capsule of fibrous tissue, they were not large or numerous enough to compress the parenchyma to a significant degree. The pelvis showed a thickened subepithelial fibrosed layer, with occasional collections of lymphocytes. The arteries and arterioles revealed no abnormality.

The ureters were elongated, tortuous and extremely dilated. The surface of the ureters was markedly congested, with many of the small veins standing out prominently. There was no obstruction along the course of either ureter. The ureterovesical orifices were patent.

The urinary bladder revealed the cystotomy opening to be well healed, with no leakage of urine around the cystotomy tube. After removal of this tube, a small amount of hemorrhagic urine was found in the bladder. The bladder wall was markedly thickened, measuring 1.5 to 2 cm. The bladder appeared to be somewhat contracted around the Pezzar catheter. The mucosa was reddish-brown in color, thickened, hemorrhagic and markedly friable. It was thrown up into prominent folds almost polypoid in appearance in many places. Although the mucosa presented a markedly hemorrhagic appearance in some areas, no ulcerations were demonstrable. The lumen of the Pezzar catheter and several areas of the mucosa revealed phosphate depositions. Microscopically, the mucosa showed acute necrosis and occasional round-cell infiltrations, the submucosa was thickened and fibrosed. Evidence of acute inflammation was absent. The muscularis contained interlacing fibrous tissue and rare perivascular collections of round cells. The adventitial coat revealed an increase in fibrous tissue, and the loose venous plexus around the bladder was thrombosed.

The prostatic portion of the urethra was patent, and the verumontanum was normal in size. Beginning at the verumontanum and extending along the course of the urethra for a distance of 3 cm was a thin, fibrosed,

valvular structure consisting of a ridge like fold extending downward from the verumontanum and dividing into two membranous sheets, the outer edges of which were attached to the rectal, lateral and pubic walls of the urethra (Fig. 5). A stream of water directed along the urethra toward the bladder produced a flattening of the valve against the wall of the urethra, indicating that no obstruction



FIGURE 5 Photograph of Urethra and Bladder Showing the Posterior Urethral Valve (V)

was present. When a stream of water was directed distally from the bladder, the valve became apparent and stood out quite prominently, producing definite obstruction. The urethra proximal to the valve appeared to be slightly dilated in contrast to the distal portion. The remainder of the penile urethra was smooth in appearance and showed no evidence of stricture or valve formations.

The penis was well formed. The scrotum was small and shrunken. The right testis was found to be adherent to the lower portion of the right ureter. The left testis was firmly bound down in the scrotum by dense fibrous adhesions. Both testes were very small and atrophic in appearance. Microscopically, diffuse fibrosis of the testes and epididymes was present. Spermatogenesis was absent. Rare, small, interstitial pigment-laden cells were seen. The ducts were not distended. Several tubules showed dark blue staining clumps, typical of calcification. The prostate was small. The vasa deferentia were not remarkable.

The parathyroid glands were enlarged (Fig. 6) and grayish-brown. The measurements and weights were as follows: left upper, 10 by 4 by 2 mm (132 mg), left lower, 11 by 7 by 5 mm (170 mg), right upper, 10 by 4 by 2 mm (90 mg), right lower, 11 by 6 by 4 mm (157 mg), combined weight, 549 mg. Microscopically, dense cords and masses of cells were seen, with a tendency toward adenomatous and papillomatous formation in some areas. Slightly enlarged chief cells predominated and

many showed vacuolization. Oxyphil cells were increased, and the intercellular fat cells were decreased in number.

Examination of the inner surface of the anterior thoracic cage revealed a series of knoblike protuberances at the costochondral junctions measuring 2 to 3 cm in diameter. Microscopically the lines of ossification at the costochondral junctions were very irregular and distorted. The junctional cartilage cells were not arranged in columnar formation. No evidence of ossification was seen in the rare proliferative cartilage cells. Adjacent to the areas of

patient as possible so that the necessary surgical treatment may be instituted. It is only by these means that renal insufficiency and the secondary changes in the bones can be prevented. In Kreitschmer's¹⁶ recently reported study of 101 cases of hydronephrosis in infancy and childhood, he found the cause for lower urinary tract obstruction in each case. He emphasized the fact that obstructing lesions at or in front of the neck of the bladder did not occur in girls. He also noted that patients came under observation late in the course of the disease, at a time when far advanced destruction of the kidneys had occurred, months or years after the diagnosis should have been made. This occurred in the case of congenital valvular obstruction of the urethra which is the subject of the present report.

Congenital valvular obstruction of the urethra is a well recognized condition¹⁷ and has been found only in the male urethra. The most severe obstructions will give rise to the earliest symptoms. In the mild cases, puberty may be reached before the kidneys are sufficiently damaged for symptoms of uremia to be manifest. In others, intractable enuresis or urinary infection may appear the latter proving to be quickly fatal or else very resistant to treatment. Marked hypertension sometimes results the patient dying from this complication before renal insufficiency has occurred.

Enuresis with or without pyuria or persistent pyuria alone demands complete urological investigation. Many observers have reported cases of dilatation of the bladder and ureters in children and have failed to investigate adequately the urethra and vesical neck for obstructive lesions. Urethroscopy is technically a difficult procedure in male children and often does not yield adequate diagnostic information. A survey of the literature failed to reveal reports of cases of renal rickets in which antenatal observations of the urethra were made.

Many of the shortcomings of urethroscopy are overcome by urethroglyphy. A technic of urethroglyphy has been recently developed and described by one of us (M. L. B.¹⁸). It is a relatively simple technical procedure which minimizes the dangers of trauma and secondary infection. Urethroglyphy gives a composite picture of the urethra from the vesical neck to the meatus and in male children will reveal meatal stricture, diverticula of the urethra, strictures, hypertrophy of the verumontanum, congenital posterior valves and contraction and relaxation of the vesical neck.

In this case, the long history of dribbling incontinence and enuresis, together with the persistent pyuria, suggested the possibility of urethral

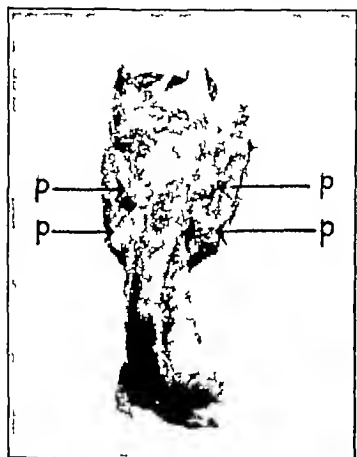


FIGURE 6. Photograph Showing Enlarged Parathyroid Glands (P)

cartilage cells were areas of extreme fibrosis extending from the cartilaginous zones into the marrow spaces of the shaft.

The heart was not enlarged or dilated and showed no abnormality of the endocardium, myocardium or coronary arteries. The aorta manifested no abnormality of its diameter or evidence of sclerotic change. There was no calcification in any of the arteries or about the joints.

The rest of the autopsy findings were negative.

In the reported cases of renal rickets, the pathological findings in the genitourinary tract have been glomerulonephritis,⁵ congenital polycystic disease of the kidneys,⁶ calculus pyelonephritis,⁷ chronic interstitial nephritis,⁸ hydronephrotic atrophy secondary to unexplained urinary retention occurring at the level of the urethrovaginal sphincter,⁹ renal calculi,¹⁰ phimosis,¹¹ congenital malformation of the urethra,¹² collar neck obstruction of the urinary bladder,¹³ congenital dilatation of the ureters,¹⁴ and congenital hypoplasia of the kidneys.¹⁵

Since many of the reported cases of renal rickets are due to congenital obstruction of the lower urinary tract it is very essential to determine the cause of the obstruction as early in the life of the

obstruction. A cystogram revealed a dilated, atonic bladder with reflux into both ureters. These findings suggested a lesion distal to the bladder. A urethrogram showed an irregularly deformed, dilated, prostatic urethra with a filling defect in its left portion, situated so as to divide the posterior urethra into two narrow irregular channels.

The autopsy corroborated the urethrographic findings of a valve in the posterior urethra as the cause of the obstruction. The bladder size was markedly diminished as compared to the cystogram taken nine months previously. This was due to the long-continued suprapubic drainage. The tone of the upper urinary tract, however, was not restored.

The unusual features about the case here discussed were the advanced age of the patient and the absence of hypertension.

The roentgenological appearance of the skeletal changes in our patient were similar to those described as "Type B" by Parsons,²¹ Price and Davie²² and others.²³

Renal insufficiency of long duration produces parathyroid hyperplasia.^{24, 25} The combined weight of the parathyroid glands of our patient was 549 mg. Microscopic examination revealed the typical chief cell, thus indicating secondary hyperplasia.²⁵ The presence of parathyroid hyperfunction was not indicated by the Hamilton and Highman test²⁶ on two occasions.* The phosphate content of the serum was increased.

SUMMARY

Clinical, chemical, roentgenological and pathological studies made on a sixteen-year-old boy, suffering from renal rickets due to renal insufficiency secondary to urinary obstruction by a congenital posterior urethral valve, are presented.

The need for careful urological investigation of children with urinary incontinence and persistent pyuria is emphasized.

The value of urethrography in the diagnosis of congenital urethral malformations is discussed.

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*The findings with the Hamilton and Highman test in this case together with a discussion of their significance have already been reported.²⁷

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ALCOHOLISM AND ATTEMPTED SUICIDE*

A Report of 143 Cases

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WHAT relation, if any, is there between alcoholism and suicide? This question has never been definitely answered and little has been written about it. Medical literature contains isolated case reports—usually incomplete—on alcoholism and suicide or attempted suicide, statistical references, usually vague and often meaningless, and moralistic articles considering alcoholism and suicide jointly or separately as vice. In the entire literature of medicine hardly more than twenty acceptable articles on this subject are recorded. So far as is known no group of cases has been presented from a clinic where fairly uniform standards of diagnosis and treatment obtained and where fairly uniform social conditions and general attitudes existed. This study, based on a survey of the records of 143 alcoholic suicidal patients admitted to the Boston City Hospital in recent years, is presented in an attempt to provide a partial answer to this question. All these patients were in the habit of drinking alcoholic liquors to excess, and were under the influence of alcohol at the time of the suicidal attempt or had attempted suicide shortly after drinking. Only a few superficial formulations about these patients as a group can be made. Nor can a differentiation be made between the alcoholic suicidal patients and the suicidal alcoholic patients, though there is certainly a distinction between the two. More detailed study of individual cases would be necessary for a deeper analysis of the problem.

Incidence

From 1915 to 1939, approximately 25,000 alcoholic patients were admitted to the Boston City Hospital. During the same period, 1195 patients were admitted after attempting suicide. Of these latter, only 143 or 11 per cent, were alcoholic. Among total alcoholic admissions at the Boston City Hospital those patients who have attempted suicide constitute an extremely minute fraction. Thus, among alcoholic cases the care of those who are suicidal is a negligible problem whereas considering all suicidal cases the alcoholic cases make up an important group. Among those patients the problem of immediate concern

is that they are suicidal and require special handling and study.

If it be true, as some writers suppose, that alcoholism and suicide represent varying forms of a self-destructive drive, one may wonder why they so seldom coincide. It appears that such a drive ordinarily may be worked out in the one form or the other, but seldom in a combination of both. It is understandable that alcohol as a more personally and socially agreeable and less strenuous pattern, should be more frequently adopted. Though alcoholism and suicide may be only symptoms

TABLE 1 Yearly Admissions According to Sex

YEAR	MEN	WOMEN	TOTAL
1915	3	0	3
1916	5	2	5
1917	5	1	5
1918	2	2	2
1919	0	2	2
1920	2	0	2
1921	1	1	2
1922	0	2	2
1923	5	1	6
1924	4	1	5
1925	10	3	13
1926	5	2	7
1927	5	1	6
1928	2	1	3
1929	5	5	10
1930	4	1	5
1931	8	1	9
1932	5	5	10
1933	12	5	17
1934	1	1	2
1935	8	3	11
1936	1	0	1
1937	1	0	1
1938	1	0	1
Totals	98	45	143

of a more fundamental personality disorder, it is clinically convenient to treat each manifestation as a syndrome and their concurrence as a syndrome.

The admission rate for the years included in this study has been fairly uniform except for a slight rise in the years 1926, 1930, 1935 and 1937 (Table 1).

Sex Distribution

In this group of 143 patients there were 98 men and 45 women (Table 1). Thus the ratio of men to women was 2:1, whereas among general suicidal patients women outnumber men in the proportion of 6:5.¹ Among all alcoholic admissions there were five times as many men as women.² Thus the sex distribution of alcoholic suicidal patients corresponds more closely to the

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group of alcoholic patients than to the suicidal group considered separately

Age Distribution

In this series the greatest number of suicidal attempts among alcoholic individuals occurred between the ages of thirty and forty for both men and women (Table 2), whereas among non-

TABLE 2 *Age Distribution by Decades*

AGE GROUP	MEN	WOMEN	TOTAL
20-30	23	13	36
30-40	35	14	49
40-50	21	9	30
50-60	12	8	20
60-70	3	0	3
70-80	2	0	2
Unknown	2	1	3
Totals	98	45	143

alcoholic suicidal patients the peak is from twenty-six to thirty for men and from twenty-one to twenty-five for women¹. There were few alcoholic suicidal patients between the ages of fifty and seventy, although among general admissions to the hospital patients in these age groups are very numerous

Previous Social Adjustment

Although all these 143 cases vary considerably in detail, appearing quite constantly in each are conditions of social maladjustment, occupational, marital or economic

The histories obtained constantly stress breakdown of the patients' personal adjustments, and development of symptomatic drinking (often in the pattern of addiction) and episodic emotional or aggressive crises often preceded by depression and bewilderment. How common these conditions are among suicidal patients who are not alcoholic it would be difficult to determine. Since this same general pattern of breakdown can and often does occur in other forms, it is interesting to note that only 4 patients in this series were considered sufficiently ill mentally to be committed as insane, although some of the other 139 patients may have been temporarily irresponsible owing to alcohol and its effects. When these patients became sober and recovered they were for the most part embarrassed and discouraged, although still obviously confronted and disturbed by various psychological and social difficulties. It is, of course, possible that many of these cases, not frankly psychotic, may have had prepsychotic personalities or may have suffered from constitutional psychopathic inferiority or hysteria

Economic Status

The patients admitted to the Boston City Hospital are for the most part those who cannot afford

private care. Nearly half of all admissions to the hospital in recent years are persons who are receiving financial aid in one form or another². Of the remainder in the top bracket, a small number of patients have an annual income of \$1500 or above

In the group considered in this study, by far the greatest number were unemployed or were of "unknown employment." Few skilled workers were included. This is due partly to the social group from which the hospital draws its patients, and partly to the personality difficulties of this particular group of patients. The pressure produced by the financial problem often appears to be a major factor in promoting a suicidal attempt. Few of these patients have shown much interest in taking advantage of the help toward adjustment offered by the Social Service Department of the hospital

Motivation

Of all the information obtained about suicidal patients, that about motivation is the most meager and unreliable. In this series 108 out of 143 patients offered no reason, probably in most cases because they were not asked for it. The stated reasons offered by 20 men and 7 women were simple and inconclusive, owing to the patients' own failure to understand their motivations, and to the lack of adequate data from which conclusions could be drawn. The reasons stated were, in broad terms: occupational maladjustment, domestic friction, drunkenness and loneliness, with resultant frustration, deprivation and anxiety. From the information obtained in this study of these patients, it appears that those in the depressive and reactive depression group understood themselves best. Those in the compulsive and hysterical groups understood themselves less well, and the schizoid and epileptoid personalities least of all. The same degrees hold true for the objective understanding of these patients by the observer

Method of Suicidal Attempt

Poison by mouth was by far the most popular method in this group of attempted suicidal cases, among both men and women (Table 3). Fifty-eight per cent of the entire group used this method. Though a wide variety of poisons were taken by mouth, iodine was by far the leader among alcoholic patients, as among all other groups¹. The ineffectiveness of iodine as a poison is probably not consciously realized by the majority of those who attempt suicide (a study of 327 cases of attempted suicide by iodine ingestion revealed no fatalities⁴). It is natural that most of

he poisons used by these patients should be substances that are common in the home and are usually marked *Poison*.

The inhalation of illuminating gas ranked second among men and among women, being the method used by 11 per cent of the patients. Other less frequently used methods were slashing, jumping from high places, hanging, immersion and firearms. Two men attempted suicide by combined methods. One patient cut his wrist and turned on the gas, and another cut his throat

quire transfer to a mental hospital after emergency treatment. In 13 the outcome was undetermined.

Only 7, 5 per cent, of the 143 alcoholic suicidal patients died in the hospital as a result of their attempts. During the same period 11 per cent of the total number of all suicidal patients died as a result of their attempts. From this it may be inferred that alcoholic patients are less successful as a group than suicidal patients in general or that alcoholism prevents suicidal patients from succeeding.

It is not easy to explain why so many of the patients in this series were unsuccessful in their attempts at suicide. It is rarely possible to state whether an attempted suicide is a gesture or is bona fide. The failures were chiefly due to the ingestion of essentially non-poisonous substances or sub-lethal doses when poisons were taken by mouth, quick and effective interference by relatives and friends after the attempt had been made, and adequate and prompt medical and surgical treatment (antidotes, gastric lavage, resuscitation, stopping of hemorrhage and so forth) at the hospital.

An additional factor, and a most important one, was the alcohol itself, which in many cases appeared to derange, inhibit or render generally less efficient the technique and planning used in carrying out the suicidal attempts. The records of these 143 cases, incomplete as they often are, give strong evidence on this last point.

SUMMARY

The findings in 143 cases of alcoholism and suicide are reported concerning the following topics: incidence, sex, age, previous social adjustment, economic status, motivation, method of suicidal attempt and outcome. The findings indicate that alcoholic suicidal patients as a group are less successful than suicidal patients in general. Attention is drawn to the meagerness of present knowledge concerning details of personality, motivation and psychological mechanisms in alcoholic suicidal patients, and to these problems in their relation to social and psychological medicine.

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TABLE 3 *Methods of Suicidal Attempt*

	MEN	WOMEN	TOTAL
Poison by mouth	49	34	83
Inhalation of gas	12	5	17
Leaping	9	4	13
Slashing	10	1	11
Hanging	8	0	8
Immersion	7	1	8
Firearms	1	0	1
Combined methods:			
Cut wrist and inhalation of gas	1	0	1
Cut throat and immersion	1	0	1
Total	95	45	143

and attempted to drown himself. No woman attempted suicide by combined methods.

Poison by mouth was the method used by 5 of the 7 patients who were successful in their suicidal attempts. No patient in this series attempted suicide by using alcohol alone, as a poison taken by mouth.

Outcome

One hundred and thirty-six, or 95 per cent, of these patients were unsuccessful in their suicidal attempts, 89 (60 men and 29 women) were discharged relieved after symptomatic treatment and a brief stay in the hospital (Table 4). Twenty

TABLE 4 *Outcome*

OUTCOME	MEN	WOMEN	TOTAL
Discharged relieved	60	29	89
Discharged at own request, against advice	16	9	25
Discharged to Nerve Service	2	0	2
Discharged to Out-Patient Department	3	0	3
Transferred to other institutions	4	0	4
Overseas undetermined	9	4	13
Died in hospital	4	3	7
Total	98	45	143

five more (16 men and 9 women) were discharged against advice before studies and treatment had been completed. Five patients, all men, were transferred to the Nerve Service or the Out-Patient Department for further treatment. Four men were considered sufficiently psychotic to re-

REPORT ON MEDICAL PROGRESS

OBSTETRICS LABOR AND DELIVERY

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ELECTIVE INDUCTION OF LABOR BY RUPTURE
OF MEMBRANES

THE physiological precipitants of labor at term, though unidentified, have long been subject to the call of castor oil and quinine, and of the bougie or bag. Before cesarean technic offered a better method, this was the chosen escape from anticipated disproportion, and even yet is frequently employed in the prophylaxis of eclampsia. Castor oil is nauseous and its results are uncertain. To quinine some parturients and some fetuses are inordinately sensitive. By its use the uterus may become hypertonic and the contractions prolonged and intense, the susceptible fetus may suffer serious damage to its auditory nerves.¹ The bougie and the bag easily introduce infection, and the former may cause retroplacental hemorrhage. Rupture of the membranes, whether spontaneous or artificial, has long been recognized as incident to both the beginning and the end of labor. During the last decade the conception of the physiology of these membranes and of their function has undergone a significant change, which has radically affected our attitude toward elective induction of labor and the methods employed for its accomplishment.

Formerly the intact bag of forewaters was considered a hydrostatic wedge which facilitated dilatation of the cervix, and "dry labors" were expected to be prolonged because the cervix had been deprived of this aid. We now believe that the os is enlarged because of an upward migration of the muscle fibers, which exert centrifugal traction on the rest of the cervix. If the intact membranes are young, tough and tenaciously applied to the internal os, this dilatation is made more difficult. The enlargement of the os proceeds without such interference when the membranes break contact with the internal os. Their degeneration with age usually accomplishes this during the last few days preceding the onset of spontaneous contractions. The same release of the cervix occurs if the membranes break or are ruptured. Many are the statistical reports²⁻⁵ asserting that labor is shorter if the membranes have opened before or

soon after the beginning of labor, and common in the experience of almost all obstetricians is the prompt recovery of progress in dilatation which had been suspended, sometimes for several hours, in the course of labor when tough membranes are broken by instruments.

In November, 1928, the exceptionally able and resourceful Dr. Delbert Jackson,⁶ after convincing experience, proposed in an address to the Boston Obstetrical Society the elective induction of labor at term in normal cases by instrumental rupture of the membranes, followed in most cases by small doses of pituitrin. Numerous authorities, especially in America, have confirmed the effectiveness of this method, and agree that the duration of labor is thereby diminished, but almost all have insisted on a few specific dangers. As there are several obvious desiderata for all those concerned in the termination of pregnancy on a prearranged date, the employment of this method is spreading widely, and has even been presented to the laity as authoritatively approved. It seems proper, therefore, while not at all condemning a procedure so helpful when used with circumspection, again to emphasize the dangers inherent in its indiscriminate application.

The statistical studies of puerperal morbidity have repeatedly shown that its incidence increases with hours of labor following rupture of the membranes. The pathological sequence is not clearly understood. Possibly the membranes themselves, which have a low resistance, are more readily infected if torn, and transmit the infection to the endometrium. Spontaneous rupture of degenerated membranes is probably commoner than that of healthy ones,⁷ and infection of the former is doubtless also more likely. The close application of the membranes to that portion of the uterus which finally becomes the rim of the dilated os must protect the endometrium from the bacteria in the cervix. A rent in the sac over the internal os possibly extends as dilatation progresses until it splits the membranes attached to the lower margin of the lower uterine segment, thus denuding the endometrium there and exposing it to infection. It appears that normally and ideally the intact ovum separates from around the periphery of the os for 1 to 3 cm. during the last

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few days before labor begins spontaneously. This lifting of the membranes may conceivably have something to do with the starting of labor, for it may involve stimulation of the sympathetic fibers of the os by the trauma of separation. We know from the study of biology and from obstetric and gynecological experience that there is a close relation between stimulation of the nerves of the internal os and the sympathetic stimulation of the pituitary gland¹⁰ which is doubtless prominently involved in labor. It would be interesting to observe the effect on selected patients at term of merely lifting the membranes from their attachment as far as the finger could reach through the internal os, together with digital pressure on the rim of the internal os. Possibly these steps alone would be effective. Very obscure is any reason why release at term of sometimes only a few cubic centimeters of amniotic fluid should be the critical factor in evoking the contractions which almost always promptly follow. The amount of liquor which escapes does not seem to be significant. Perhaps it is equally insignificant whether or not any escapes.

We dwell on this detail for there is danger of infection with prolonged labor after rupture of the membranes. If the purpose for which elective rupture is done at present could be fulfilled without it, induction would be safer. Until such time, the considerate and perspicacious physician will not select for induction by present methods a patient whose long, firm cervix presages a lengthy first stage of labor, nor apply the procedure to any patient until approach to term has effected a partial effacement, softening and dilatation of this crucial organ.

Nor is this expedient available in any pregnancy at term with possible disproportion or abnormal presentation. In either case labor may be prolonged or preferably terminated by delivery from above. Although the improved technic of extraperitoneal approach which Waters,¹⁰ of Jersey City has proposed (see below) and will soon present in the literature notably diminishes the risk of cesarean section following so-called dry labor, it remains more than folly wilfully to expose a patient to certain risk for the sake of a theoretical escape. Prolapse of the cord with vertex presentations is rare unless intrafundal manipulation usually for rotation or version, lifts the head above the inlet. Elective induction by rupture is hardly defensible if anything but the vertex is presenting in a clearly adequate pelvis. It is as yet approved by its more judicious proponents only when in such cases of normal presentation without a suggestion of disproportion the pregnancy is at term and the cervix is short

soft, already patulous and without a previously acquired reputation for dystocia.

RELIEF OF PAIN DURING LABOR

In spite of a few voices whose calling would sound better in the pre-Victorian wilderness of midwifery than in modern medical discipline, endeavors to make labor painless as well as safe and productive still proceed. One woman physician¹¹ says "Childbearing is so essential an experience to a woman that the thwarting [*sic*] of its normal course by the excessive [*sic*] use of analgesics may cause damage to her personality. An eminent obstetrician¹² with no discernible evidence of tongue in cheek writes: Actually, I have often felt that the women miss something when they are delivered under an anesthetic—the thrill of hearing their baby's first cry. Labor must be tame for these women. Defying the published statistics from several clinics, rather exceptionally equipped with talent and facilities, to be sure, he later says: 'Neither in theory nor in practice is there a harmless anesthetic or analgesic. Intelligent and discerning physicians may not condemn such statements, but neither are they impeded by them. The propriety of relieving any useless, purposeless pain, even though it be associated with such an instinctive and passionately sentimental function as reproduction, needs no argument. If the partial achievement of such relief as is rapidly becoming the case with discriminating analgesia during labor diminishes the net mortal danger, it becomes obligatory.

Chloroform and ether alone were boons in their time; nitrous oxide was a welcome addition. Novocain has its special uses. Morphine and scopolamine, at a price, showed how comfortable labor could be made. Now the barbiturates^{13, 14} and paraldehyde¹⁵ take an honored place among these merciful agents. They are all potentially dangerous, to be sure, but so is digitalis, and even ethyl alcohol. Like these latter drugs, they must be used with close regard to their toxic effects on patients whose peculiarities both of constitution and of medical condition are known to offer no contraindication. Thus precautions are taken to prevent evil results as facilities are also held ready to relieve any unexpected disturbances.

The experience in many clinics during the last decade currently present these conclusions:

1 Morphine, $\frac{1}{2}$ gr., or pantopon $\frac{1}{2}$ gr., enhanced by scopolamine, 1/200 to 1/100 gr., repeated alone or together as necessary at intervals of three or four hours is helpful during the first stage of primiparous labor. Morphine or pantopon must not be given unless one is reasonably sure

that delivery will not occur within four hours, because of their depressant effect on the fetal respiratory center. They are therefore not often useful during the second stage of labor or for multiparas.

2 Barbiturates are more safely given by mouth or by rectum than intravenously, although their action is thereby slightly delayed. Pentobarbital and Sodium Amytal are the popular forms, and of these the former acts more quickly and in smaller doses. From 4 to 6 gr is given, preferably with scopolamine, 1/200 to 1/100 gr, when contractions are well established, and if possible before they become acutely distressing. Pentobarbital, 1½ to 3 gr, is repeated at intervals of three or more hours, or as the patient becomes wakeful, scopolamine, 1/200 gr, is given every three or more hours if she is rational. Barbiturates given by mouth are not dependable if the stomach contains much recently ingested food. Complete narcosis with barbiturates must not be induced by any route if the stomach contains food, for vomitus is often expelled with difficulty, a fact which makes inhalation of food particles easily possible.

3 In addition to the barbiturates and scopolamine, in order to allay undue restlessness, paraldehyde in doses of 4 to 8 cc may be given by rectum with 30 or 60 cc. of ether in an equal amount of olive or cottonseed (not mineral) oil, once or twice toward the end of the first stage.

4 Nitrous oxide and oxygen, in proportions of 10 or 15 l, are given during the second stage, and a modicum of ether is added, if necessary for delivery.

5 For obvious reasons the patient must never be without competent, contiguous supervision.

6 While barbiturates are not contraindicated in mildly abnormal cardiac conditions, the rare patient whose cardiorespiratory system is unduly sensitive to them, and who therefore develops pulmonary edema, must be promptly supplied with oxygen by tent or mask.

7 The newborn baby, after barbiturates and scopolamine have been used, may not at once cry or even breathe deeply. He may be stimulated, but very gently, as by rubbing or patting on the back, pinching the toes, or immersing the buttocks momentarily in cold liquid. All babies should be drained, and the mucus in the pharynx should be aspirated. Time and delicate appropriate attention will ensure their proper behavior if they have not been unduly traumatized by delivery or smothered by too rich a mixture of nitrous oxide and oxygen. The beginning of normal respiration is encouraged and accelerated by administering oxygen for a short time immediately after ligation of the cord.

It may be deduced from the above that the degree and the safety of obstetric analgesia with the agents at hand critically depend on the ability of the attending physician accurately to perceive the peculiarities of each patient, as well as those of her obstetrical condition and of the quality of her labor, and to apply these agents accordingly. Furthermore, it is clear that the exigencies of such procedures, both maternal and fetal, justify their use only in thoroughly equipped hospitals. Bad results under other conditions call not for the repudiation of analgesia, but rather for improvement of these conditions.

OCCIPITOPOSTERIOR PRESENTATION

Perennially the literature is replete with discussions of treatment of presentation with the occiput posterior. Conservative expectancy is the dominant note. Steadily the experience of able operators convinces us that time and good contractions will result in the rotation of about 80 per cent of posterior vertices when they reach or press on the perineum. The supervised use of analgesics as outlined above makes infinitely easier the strain of delay, which too often in the past was more than the patient or the harassed accoucheur could withstand. Manual rotation of head and shoulders is not difficult in many cases in which spontaneous adjustment fails as the cervix becomes fully dilated. If this has not been accomplished and a posterior vertex is arrested on or near the perineum, some will still no doubt apply forceps twice, according to the method of Scanzoni. This procedure is fast passing from conventional use, since high and mid-forceps are avoided by the tolerance of prolonged but painless labor. Commoner now is the simple method of rotating the blades after cephalic application to a low head. Paine,¹⁶ using Simpson forceps without traction, describes his excellent method as follows:

1 Time spent in thoroughly dilating the pelvic floor is more than saved in the case of subsequent proceedings.

2 The left blade is applied anteriorly, starting directly under the symphysis with the handle held to the right of the midline and practically at right angles to the floor. The head is pushed back from the symphysis and the blade guided by a finger through the fenestra.

3 When the blade has reached its approximate correct position, the handle is held temporarily to the left to permit room for the application of the posterior (right) blade.

4 The application of the posterior blade begins with the handle held parallel to the right Pouparts, the handle depressed as the blade follows up the hollow of the sacrum. As the blade comes into approximate position, care is taken to keep the handle well toward the right thigh.

5 The handle of the left blade is now brought over to the right and locked with the right blade.

6. The relation of posterior fontanel and sagittal suture to the blade is noted to indicate a correct cephalic application. Traction is not attempted until a correct application is secured.

7 Beginning traction is sharply downward, in a line as near right angles to the floor as possible, taking extreme care to keep the handles well to the right of the midline. This is necessary to keep the tips of the blades to the left side of the pelvis, i.e., over the face.

If traction is made with the handles in the midline, the blades are thrown over to the right, toward the occiput and if they do not catch under the mastoids will often slip off over the occiput.

BREECH PRESENTATION

Graufing in the experience of many writers are the results of external version during or at the end of the eighth month. Advising against the use of anesthesia, which may permit unduly vigorous efforts, most commentators mention the advantage of the extreme Trendelenburg position and of gentleness. If the breech must be born, fortunately at last there is general agreement that it should be allowed to deliver spontaneously, almost always through an incised perineum, unless practically constant osculation during the second stage detects dangerous fetal embarrassment. Most operators prefer to deliver the trunk by gentle traction on the legs and hips, wrapped in a warm moist towel, ending its delivery with the back uppermost. When the anterior scapula is visible, whichever arm comes out easier is delivered first. Usually this is found to be the anterior arm and occasionally it has seemed simpler to rotate the shoulders gently so as to bring the second arm also to the anterior position. Before any attempt is made to deliver the head, the right handed operator is still advised to apply the index and middle fingers of the left hand to the fetal face in order to ensure flexion. If pressure on the vertex from above toward the floor with no more than the gentlest traction on the body fails to produce the head, the use of forceps, carefully and deliberately applied is uniformly recommended. Emphatic caution against haste and vigor is given repeatedly.

PROPHYLACTIC PERINEOTOMY

The refreshingly precise Phaneuf¹⁷ has called attention to the impropriety of applying the word "episiotomy" to discussion of the perineum. Dorland¹⁸ defines episiotomy as "the surgical incision of the vulvar orifice laterally for obstetrical purposes." The distinction is useful for correct use of the word will dispense with the impossible qualification "median" and the redundant "lat-

eral." Happily there is less confusion in the application of the procedure. The prophylactic value of perineotomy, the so-called "median episiotomy," has been frequently affirmed in recent papers from various sources. Its use presupposes adequate surgical facilities for strict asepsis, and personal ability. In the absence of either local infection is frequent, and if it does occur, is annoying and embarrassing. Symmetrical separation of the perineal body practically always protects the vaginal epithelium from the undesirable laceration of the gutters, which can usually (not always) be attributed to poor technique in the application of low forceps. The operator must furthermore be alert and promptly divide one of the levators laterally if protection of the sphincter demands more room. Repair of the muscle layers is easy with three or four interrupted sutures of even No. 00 chromic catgut. The same material may be used as a subcuticular running stitch to close the vaginal epithelium and the skin of the perineum. As the elimination of exposed knots contributes much to the patient's comfort one may prefer to anchor the continuous sub-epithelial suture by starting at the posterior end of the perineal wound and working anteriorly to finish with a knot in the vagina. Nice approximation of edges is easier if closure begins at the peak of the separation of the vaginal epithelium and terminates at the posterior end of the perineal wound. In order to protect the sensitive skin edges from a knot there which would catch in gauze, one may bring a final stitch out through the skin 1 or 2 cm. lateral to the approximated cut edges. This stitch is kept from retracting by a knot placed close to the exposed surface of the skin. The already stipulated indispensability of asepsis and technical skill is obvious.

CESAREAN SECTION

Although the time has not yet arrived when one can demonstrate the startling contention of some obstetricians that abdominal delivery for the safety of mother and child should supplant all but the simplest of operative vaginal deliveries, current trends and statistics offer seductive considerations. With improvement in general surgical technique and facilities, and in postoperative care, diagnosis and therapeutic resources, the mortality of cesarean delivery in first-class clinics has gradually diminished in the last twenty years to 2 or 3 per cent although the numbers of patients delivered from above may even have increased. Meanwhile the incidence of high forceps, and in many clinics that of versions, has also diminished. This is partly due to better acquaintance with and more dependence on the nat-

ural forces of labor, and partly, as has already been said, to the fact that safe analgesia permits prolonged submission of patient and physician to slow progress. That fewer patients suffer difficult pelvic deliveries is also due, however, to more accurate identification of disproportion, and readier selection of abdominal delivery in these cases, as well as in cases of transverse position and of placenta previa. (Only for toxic separation of the placenta has vaginal delivery finally gained preference over the previously favored cesarean¹⁹) This freedom of cesarean election is largely attributable to improvements in operative methods. Obviously desirable and equally attainable is partial or complete exclusion of the upper abdominal cavity. The approach most commonly selected is still transperitoneal but leads to the lower uterine segment or cervix, where healing is somewhat easier and subperitoneal seclusion of the wound quite simple. Many operators routinely protect the abdominal cavity by suturing a flap of uterine visceral peritoneum to the anterior parietal layer before incising the uterus. The simplest routine precaution is separation of the upper abdominal regions from the operative field by generous packing. The relative merits of transverse and longitudinal incision through the musculature are not clearly apparent in the literature. Both have their eminent protagonists. (The reviewer favors the transverse incision but is deliberate in avoidance of lateral vessels, meticulous in closure of the wound, and fearfully fussy at both its ends.)

The Latsko extraperitoneal approach has served capable surgeons well, and has saved either the uterus or the baby for many patients who were adjudged infected, perhaps by long labor with ruptured membranes, or by previous attempts at delivery. The technic is not easy in practice and threatens the bladder, ureters and large vessels, somewhat in proportion to the operator's facility or experience.

In order to avoid these disadvantages, many will henceforth use a new method which was reported to the New York Obstetrical Society in

January, 1939, and to the Boston Obstetrical Society in March, 1939, by Doctor Edward G. Waters,¹⁰ of Jersey City. He convincingly demonstrated the feasibility of exposing the lower uterine segment by extraperitoneal approach in the midline between the parietal peritoneum and the bladder, and laterally through the infraperitoneal areolar tissue. Because he has not yet published his excellent method it would be unseemly to detail it further. Let the reviewer rest with acclaim to Doctor Waters for a very promising improvement, and with exhortation to him to hasten its literary appearance and to obstetricians to give it prompt, judicious attention.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Stated Meeting, October 4, 1939

A STATED meeting of the Council of the Massachusetts Medical Society was held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 4 at 10.30 a.m. The president, Dr Walter G Phippen, Essex South, was in the chair, and 188 councilors were present (Appendix No 1)

The records of the annual meeting of June 7, 1939, were presented by the Secretary as published in the *New England Journal of Medicine* issue of June 29, 1939. No errors or omissions being noted the records were approved as printed.

REPORTS OF STANDING COMMITTEES

Arrangements

The chairman, Dr Augustus Thorndike, Jr., Suffolk, made an informal report in which he stated that the committee had held two meetings, one of which was attended by the officers of the Society and the chairmen of the various sections. It is proposed to hold the annual meeting of 1940 on May 21 and 22 at the Copley Plaza Hotel in Boston. The plan contemplates two full days in place of the previous two-and-a-half-day session. There is to be a continuous scientific program from 9 to 12 and 2 to 5 each day. The meeting of the Council the Board of Censors and the Cotting Luncheon are to be held on the first day, with the annual dinner followed by the Shattuck Lecture in the evening. The annual meeting of the Society and the luncheon will be held at noon on the second day. It is hoped to be able to adjourn the meeting at 5.00 p.m. on the second day. The Council voted to adopt the report and subsequently voted to adopt the recommendations of the committee.

Ethics and Discipline

The report (Appendix No 2) was presented by the chairman, Dr Robert L. DeNormandie, Suffolk, and was accepted by vote of the Council.

State and National Legislation

A report was presented informally by the chairman, Dr Charles C Lund, Suffolk. He said that the committee had followed pending legislation up to the end of the legislative session about August 1. Since the last report of the committee, the nurses bill had been defeated, and in the opinion of the chairman the medical profession should act with the nursing group and help to plan a

bill for submission to the next assembly of the Legislature. He added that the present act governing the practice of nursing is much in need of revision.

Of the two syphilis bills, originally introduced by Dr Harry M Landesman, Norfolk, one was passed, hence, from the first day of November, a blood test for syphilis must be taken at the first visit of all pregnant women to a physician. No penalty is attached, but it is apparent that the public expects a careful examination in all such cases.

The bill introduced by the Society, proposing to set up a form of medical insurance, failed to pass the Senate Rules Committee largely because of the confusion in the legislative program. In the chairman's opinion this was probably fortunate, since such a bill should have very careful consideration and should not be rushed through the Legislature. He suggested that all members of the Society should study the proposed bill carefully in a critical spirit so as to discover its weaknesses. He doubted whether the proposed bill actually provided sufficient protection for the proposed organization, since there are insufficient restrictions concerning the physicians who would be permitted to work under the bill. He quoted from the California experience where each physician desiring to work under the provisions of the bill has to pay a five-dollar fee, in that way providing funds with which to begin operations.

He reported that the Wagner Bill was not passed at the last session of Congress, but that Senator Wagner would undoubtedly introduce a bill in a somewhat different form, in order to meet certain points which have been adversely criticized by different groups.

He reported that Senator Henry Cabot Lodge, Jr., of Massachusetts had introduced a bill (Senate No 2963) which may be regarded as an "entering wedge." This bill begins by undertaking to meet a small part of the problem of medical care but might be expanded later into something larger. In the chairman's opinion this is probably a step along the lines insisted on by the American Medical Association as proper for the government to pursue. The bill provides for benefits, under certain conditions to certain people who are insured under the Social Security Act to the extent of twenty five dollars per year. The act would be administered by the Social Security Board. In his opinion this bill should be care

fully studied before it comes up in Congress at the next regular session

The Council voted to adopt the report

Membership

The report (Appendix No 3), which was presented by the chairman, Dr H Quimby Gallupe, Middlesex South, recommended that seven fellows be allowed to retire, three allowed to resign, one be deprived of the privileges of fellowship and one be recommended for affiliate fellowship in the American Medical Association. The Council voted to accept the report and to approve the committee's recommendations

Public Health and Subcommittee on Public Education

The report (Appendix No 4) was presented by the chairman, Dr Francis P Denny, Norfolk, and was accepted by vote of the Council

Medical Defense

The report was presented informally by the chairman, Dr Arthur W Allen, Suffolk. He stated that there has been a marked diminution in the number of suits instituted against physicians. In the chairman's opinion this has been due to the fact that each suit brought has been opposed and that no suit has been settled. There has also been widespread publicity among the profession concerning the ease with which a malpractice suit may be started. He called the attention of the new councilors to the importance of being on the alert for any rumors concerning the institution of a malpractice suit. He announced that it will continue to be the policy of the committee to carry on the old principle of fighting each suit. Since the first of June only one suit has been brought, and it is believed that this will be withdrawn as soon as the attorney discovers that the Massachusetts Medical Society will defend it. The report was duly adopted

Others

There were no reports from the Committee on Publications, the Committee on Medical Education and Medical Diplomas, the Committee on Permanent Home and the Committee on Financial Planning and Budget

REPORTS OF SPECIAL COMMITTEES

Postgraduate Instruction

The report (Appendix No 5) was presented by the chairman, Dr Frank R Ober, Suffolk. The Council voted to adopt the report

Industrial Health

The report (Appendix No 6) was presented by the chairman, Dr W Irving Clark, Worcester. It was duly adopted

Restoration to Fellowship

The reports of the committees previously appointed to consider petitions for restoration to fellowship were accepted, and the recommendations to restore the following five fellows were approved by the Council

Emile A Barrier, Belmont (Committee Donald E. Currier, Leo A Blacklow and Fabyan Packard)

David Barron, Brockton (Committee Alfred L Duncombe, Fred F Weiner and Harrison A Chase)

I L Kushner, Somerville (Committee Edmund H. Robbins, C Howard Dalton and Louis J Grandison)

John F O'Brien, Fall River (Committee Edward L. Merritt, George C King and Emery C Kellogg)

Harold S Tait, Palmer (Committee Morgan B. Hodskins, Sidney R. Carsley and Lucy G Forrer)

Others

There were no reports from the Committee on Cancer, the Committee on Physical Therapy and the Committee on Public Relations

APPOINTMENTS AND CONFIRMATION OF COMMITTEES

The Auditing Committee chosen consists of Dr Ezra E Cleaves, Essex South, as chairman, and Dr Edwin B Dunphy, Suffolk

The President announced his appointment of the committee to support an appropriation by Congress for the construction of a new building to house the Army Medical Library and Museum as follows

Henry R. Viets, Suffolk, *Chairman*

Robert B Osgood, Suffolk

Benjamin Spector, Suffolk

The President nominated and the Council approved of a committee to study the practice of medicine by unregistered persons as follows

Richard Dutton, Middlesex East, *Chairman*

Brainard F Conley, Middlesex South

Edward F Timmins, Suffolk

Interim Appointments

The following nominations by the President were approved by the Council. Dr Peer P Johnson, of Beverly, as a member of the Council to succeed Dr Walter G Phippen, Essex South, Dr Johnson to be a member of the Committee on Financial Planning and Budget to succeed Dr Phippen, and Dr Archibald R Gardner, Middlesex North, to be one of the voting members of the Associated Hospital Service Corporation of Massachusetts

INCIDENTAL BUSINESS

The President referred to a recommendation from the Advisory Committee of the Section of Obstetrics and Gynecology to appoint a committee of five to study the question of expert testimony

in court cases. He stated that such a committee was appointed by the Council in October, 1936, but that the committee had never reported and had never been discharged from its duties. He announced that this committee would be asked to render a report. The committee consists of the following:

George L. Schadt, Hampden *Chairman*
David Cheever, Suffolk
Francis P. McCarthy, Norfolk
Walter G. Phuppen, Essex South
James J. Goodwin, Worcester

Upon motion of the Secretary, seconded by Dr. David Cheever, Suffolk, the Council voted to publish the *Directory of the Officers and Fellows* as of February 15, 1940, at a cost of approximately \$2000.

At the June meeting of the Council, Dr. John Fallon, Worcester, had presented a statement on the status of anesthetists under the Hospital Prepayment Plan. The Secretary read a communication from Dr. Wiggan enclosing a copy of the statement asking that it be referred to the proper authorities for final consideration. After some discussion Dr. Channing Frothingham, Suffolk, stated that during the past summer the Associated Hospital Service Corporation had revised its policies and that the new ones have excluded anesthesia from the benefits so that there is no need for further action on Dr. Fallon's reports.

Dr. Henry M. Landesman, Norfolk, referred to the two bills introduced into the Legislature last year by him. One of these bills was passed but the one having to do with the prenuptial test was lost. He therefore introduced a resolution (Appendix No. 7). After some discussion the Council voted to refer the resolve to the Committee on Public Health.

Dr. John B. Hall, Norfolk, asked for information from some member of the House of Delegates or from the trustee of the American Medical Association, Dr. Roger I. Lee, concerning the disposal of a question which had arisen in the House of Delegates at the last annual meeting of the American Medical Association. This concerned the omission of the designation "col" which has appeared in the *American Medical Directory* following the names of colored physicians. Dr. Lee in reply stated that the Board of Trustees at its last meeting had voted to omit this designation in the next directory.

The President stated that there was no provision in the bylaws which required a report to the Society from the delegates chosen to attend the annual meeting of the American Medical Association. In his opinion such a report might be valuable but is not necessarily essential since the full proceedings of the House of Delegates are regularly published in the *Journal of the American Medical Association*, together with such votes as

may be taken. The full report is therefore available to all members of the Massachusetts Medical Society.

The meeting adjourned for the Cotting Lunch at 11:36 a.m.

ALEXANDER S. BEGG, *Secretary*

APPENDIX NO. 1

ATTENDANCE

BARNSTABLE	J. H. Blaisdell
M. E. Champion	Richard Dutton
BREKSHIRE	E. M. Halligan
J. J. Boland	J. H. Kerrigan
J. S. F. Dodd	K. L. MacLachlan
	R. W. Sheehy
BRISTOL NORTH	MIDDLESEX NORTH
R. M. Chambers	F. L. Gage
W. H. Allen	M. L. Ailing
F. H. Dunbar	A. R. Gardner
W. H. Swift	G. A. Leahey
BRISTOL SOUTH	E. A. Payne
G. W. Blood	C. M. Roughtan
E. D. Gardner	M. A. Tighe
H. E. Perry	
J. N. Tilden	MIDDLESEX SOUTH
C. C. Trapp	Dwight O'Hara
P. E. Truesdale	C. F. Atwood
ESSEX NORTH	E. W. Barron
E. S. Bagnall	W. B. Bartlett
R. V. Baketel	Harris Bass
C. S. Benson	E. H. Bigelow
E. H. Ganley	G. F. H. Bowers
H. R. Kurth	E. J. Butler
P. J. Look	B. F. Conley
G. L. Richardson	D. F. Cummings
F. W. Snow	C. H. Dalton
L. T. Stokes	H. F. Day
C. F. Warren	C. L. Derick
C. A. Weiss	J. E. Dodd
ESSEX SOUTH	H. Q. Gallupe
N. P. Breed	H. G. Giddings
C. L. Curtis	H. W. Godfrey
S. E. Golden	W. G. Grandison
J. F. Jordan	A. D. Guthrie
B. B. Mansfield	A. M. Jackson
W. G. Phuppen	A. A. Levi
J. R. Shaughnessy	A. N. Makechnie
	R. A. McCarty
	J. A. McLean
FRANKLIN	Edward Mellus
F. J. Barnard	J. C. Merriam
W. J. Pelletier	C. E. Mongan
H. G. Stetson	J. P. Nelligan
	W. D. Reid
HAMPDEN	Max Ritvo
Frederic Hagler	E. S. A. Robinson
T. S. Bacon	E. F. Ryan
W. C. Barnes	M. J. Schlesinger
J. L. Chereskin	W. N. Secord
E. C. Dubois	E. F. Sewall
M. F. Gaynor	E. W. Small
M. W. Pearson	H. P. Stevens
A. G. Rice	R. A. Taylor
	R. H. Wells
MIDDLESEX EAST	M. W. White
C. R. Balsley	W. S. Whittemore

NORFOLK

C. J. Kickham
J. D. Adams
W. W. Barker
A. S. Begg
D. N. Blakely
Myrtelle M. Canavan
F. P. Denny
G. L. Doherty
Albert Ehrenfried
D. G. Eldridge
C. B. Faunce, Jr.
Maurice Gerstein
W. A. Griffin
J. B. Hall
H. L. Johnson
C. J. E. Kickham
E. L. Kickham
H. M. Landesman
D. L. Lionberger
D. S. Luce
D. L. Lynch
F. J. Moran
M. W. O'Connell
D. D. Scannell
J. W. Spelman

NORFOLK SOUTH

C. S. Adams
G. V. Higgins
H. A. Robinson

PLYMOUTH

A. W. Carr
P. B. Kelly
P. H. Leavitt
W. H. Pulsifer

SUFFOLK

Reginald Fitz
A. W. Allen
H. L. Blumgart
W. B. Breed
W. J. Brickley
W. E. Browne
C. S. Butler
E. M. Chapman
David Cheever
M. H. Clifford
R. L. DeNormandie
N. W. Faxon

G. B. Fenwick
Channing Frothingham
Joseph Garland
John Homans
Rudolph Jacoby
H. A. Kelly
T. H. Lanman
R. I. Lee
C. C. Lund
G. R. Minot
W. J. Mixer
J. P. Monks
R. N. Nye
F. R. Ober
J. P. O'Hare
L. L. Phaneuf
Helen S. Pittman
W. H. Robey
R. M. Smith
M. C. Sosman
Augustus Thorndike, Jr.
S. N. Vose
Shields Warren
Conrad Wesselhoeft

WORCESTER

J. C. Austin
Gordon Berry
W. P. Bowers
L. R. Bragg
*W. I. Clark
G. A. Dix
E. B. Emerson
G. E. Emery
J. M. Fallon
J. J. Goodwin
E. R. Leib
W. F. Lynch
J. C. McCann
J. W. O'Connor
W. C. Seelye
C. A. Sparrow
G. C. Tully
R. J. Ward
F. H. Washburn
S. B. Woodward

WORCESTER NORTH

B. P. Sweeney
E. A. Adams
C. B. Gay
J. C. Hales

*By invitation

APPENDIX NO 2

REPORT OF THE COMMITTEE ON ETHICS AND DISCIPLINE

Since our report to you in June the committee has held four meetings, all of which the president of the Society attended. Eleven new complaints have been received. Eight of these, all minor in character, were satisfactorily adjusted after careful investigation and need not be gone into here.

One fellow, who was convicted in a court of law of a crime and from whom a written request for a hearing has not been received, is recommended for deprivation of fellowship by the Council under Chapter I, Section 8 (c), of the by-laws. The report will be presented to you for action by the Committee on Membership.

A complaint was made against a fellow by a patient

who had been seriously injured in an automobile accident. The complainant stated that he had received from the fellow a large bill for services rendered to him while he was in a hospital and for appearing in court. The complainant stated that he had refused to pay the fellow's bill as he believed that it was unjust. The complainant further stated that the fellow had attached the award given him by the jury and that he had been put to considerable expense in trying to have the fellow's bill reduced and the attachment removed, without avail. After a long and complicated investigation by the committee we gave the fellow a hearing, at which it was conclusively proved that the bill was unjustified and that there was a serious error in the amount of the bill, we criticized him for attaching the award that was given to the patient. At the hearing the fellow admitted that the bill was wrong. We gave him the opportunity to rectify his error and the injustice that he had done to the patient. He at once instructed his lawyer to make amends. The complaint before us was withdrawn immediately by the complainant. After considerable discussion in the committee, we recommended that the President give the fellow a very severe admonition, and this has been done.

Another hearing was on a complaint from two fellows of the Society against two other fellows because of medical testimony that the latter had given in a lawsuit against the complainants. We gave a hearing to the two fellows against whom the complaint was made, and after extended hearings and much discussion the committee finally voted unanimously to ask them to resign from the Society. Their resignations have been received.

ROBERT L. DeNORMANDIE, *Chairman*

APPENDIX NO 3

REPORT OF THE COMMITTEE ON MEMBERSHIP

This committee recommends

1 That the following named seven fellows be allowed to retire under the provisions of Chapter I, Section 5, of the by-laws

Briggs, J. Emmons, North Dighton
Felch, Carrie I, Boston
Felch, Lewis P, Boston
Godfrey, Joseph W, Swampscott, with remission of dues for 1938 and 1939
Karr, George W, Sharon
Little, Abby N, Laconia, New Hampshire
May, James V., Watertown

2 That the following named fellow be allowed to resign under the provisions of Chapter I, Section 7, of the by-laws

Rhoad, Owen W, Windsor, Vermont

3 That the following named retired fellow be recommended for affiliate fellowship in the American Medical Association

Wilcox, DeWitt G, Newton Centre

4 That the following named fellow be deprived of the privileges of fellowship under the provisions of Chapter I, Section 8 (c), of the by-laws

Vassallo, John E, Malden

5 That the resignations of the following named fellows be accepted under the provisions of Chapter VII, Section 4, of the by-laws

Donaghy, G. Everett, Cambridge
Marvin, Frank W, West Newton

H. QUIMBY GALLUPE, *Chairman*

APPENDIX NO 4

REPORT OF THE COMMITTEE ON PUBLIC HEALTH
AND THE SUBCOMMITTEE ON PUBLIC EDUCATION

The committee has arranged for the continuation of the radio talks, "Green Lights to Health" during the coming year. These broadcasts will be on Wednesdays at 4 p.m. over WAAB. On account of the "World Series" the first talk cannot be given until October 18. The program with titles of addresses and speakers has been completed through December.

A request from a Rotary Club for a talk on the subject of "Socialized Medicine" has been fulfilled.

FRANCIS P DENNY *Chairman*

APPENDIX NO 5

REPORT OF THE COMMITTEE ON POSTGRADUATE INSTRUCTION

Since the annual report of the postgraduate extension courses to the Council last June, the committee closed the fiscal year with the government agencies on June 30 1939. The funds appropriated for postgraduate extension courses by these agencies were \$7422.85. The Society in February 1939 appropriated an additional \$1000 which is being used at the present time to help defray clerical printing and administration expenses. At the end of the calendar year a report of the disposition of this fund will be made to the Council.

In July 1939 arrangements were made through Dr Paul J Jakmau state commissioner of public health, to continue the postgraduate extension courses for the current academic year 1939-40. Curricula have been made out and sent to the respective districts. Ten districts will have the courses this fall and the remainder later in the year.

The New England Postgraduate Assembly has been organized in co-operation with the medical societies of Maine, New Hampshire, Vermont and Rhode Island. The program has been published in the *New England Journal of Medicine*. An invitation program will be mailed to each registered physician in the sponsoring states this week. The program has been completed and will be given as published, with the exception that Sir Thomas Lewis, of England, has been forced to cancel his appointment due to the current European war. He sends his regrets to the Society. Dr Lewis A. Conner of New York City will fill the place of Sir Thomas on the program.

The committee expresses appreciation and thanks to all the district chairmen who are actively carrying on the organization work in their communities. The time and place of the extension courses will be announced each week in the columns of the *New England Journal of Medicine* as well as the speakers names and the titles of the lectures.

FRANK R. OREN *Chairman*
LEROY E. PARSONS *Secretary*

APPENDIX NO 6

REPORT OF THE COMMITTEE ON INDUSTRIAL HEALTH

The Committee on Industrial Health was appointed April 27 1939. Immediately after its appointment the committee contacted the Council of Industrial Health of

the American Medical Association. The secretary of the Council suggested that our committee make certain contacts in Massachusetts and elsewhere. The following contacts have been made

- 1 National Industrial Conference Board
(Conference Board of Physicians in Industry)
- 2 National Association of Manufacturers
(Committee on Healthful Working Conditions)
- 3 Air Hygiene Foundation of America Pittsburgh
- 4 Harvard School of Public Health
(Department of Industrial Hygiene)
- 5 Massachusetts Department of Labor and Industries
(Division of Occupational Hygiene)
- 6 Liberty Mutual, Arrow Mutual and other insurance companies in Massachusetts providing workman's compensation insurance.

The committee was asked by the secretary of the Council to provide information on many phases of industrial medicine and industrial hygiene in Massachusetts, including a list of the physicians doing full-time or part-time industrial work. All questions have been answered, and the list requested has been made out and sent.

The committee expresses to the Secretary its appreciation of his help in obtaining this list of names.

The committee has had several meetings and is working on a program for future work. It is at present preparing a description and a discussion of the physical examination in industry. A committee of lay and medical men in Wisconsin has recently issued such a report, which was developed under state influence. The report is well done and suggests that a similar report might be of value to the members of this society who are practicing industrial medicine.

W IRVING CLARK, *Chairman*

APPENDIX NO 7

RESOLUTION PRESENTED BY DR. HENRY M. LANDESMAN

WHEREAS, More than half of the states in the Union have adopted prenuptial health laws during the past four years and

WHEREAS, There is a national drive being waged against syphilis and gonorrhea by Surgeon-General Parran and

WHEREAS, The Legislature in this commonwealth has not been willing to pass prenuptial-serological-blood-test legislation during the past four years and

WHEREAS, It has been definitely proved that syphilis and gonorrhea, when discovered, can be uprooted and innocent individuals at least can be protected from contracting the above diseases and

WHEREAS, Since a prenatal-serological-blood-test bill was passed by the last Legislature and signed by the Governor, it is advisable to take advantage of this fact and utilize this opportunity even in an educational way by having the Council adopt the following resolution and sponsor its purposes and results therefore, be it

RESOLVED That the Massachusetts Medical Society adopt and sponsor this resolution that all couples about to be married should have a general physical examination or at least a serological blood test for syphilis.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25441

First Admission A forty-six-year-old, married Canadian was admitted to the hospital complaining of difficulty in breathing.

Six months before entry he noted the onset of progressively increasing orthopnea, and eventually had to sleep propped up. At the same time he experienced a dragging feeling in his abdomen. Five months before entry he noted swelling of the ankles but did not recall whether they were less swollen in the morning after a night's rest. Throughout this six months' period he experienced great difficulty in breathing on exertion so that two weeks before admission a single step caused him to become breathless. He was able to maintain employment as a solderer during this time simply because of the lack of physical exertion which this work entailed. He was placed on a reducing diet and given thyroid extract, two pills daily, until two weeks before admission when the number was increased to three, but his weight remained about 250 pounds. During his present illness he had been given "green pills" for his heart, of which he took three daily. Because of his steadily progressing symptoms he entered the Out Patient Department for relief and was immediately referred to the hospital. He denied the following symptoms, hemoptysis, chest pain, palpitation and paroxysmal nocturnal dyspnea.

The patient believed that during childhood he had had measles, mumps, pertussis, chickenpox, scarlet fever and possibly diphtheria. He denied ever having had rheumatism, rheumatic fever or kidney trouble but had had frequent sore throats. He had successfully undergone an appendectomy seventeen years previously. Starting ten years before entry he had gradually climbed in four years from about 170 to 250 pounds in weight, at which weight he had remained. He had experienced nocturia two times regularly for the past six years, which had not changed significantly during the six months previous to his admission.

Physical examination revealed a very obese, slightly cyanotic man sitting up, with slightly wheezing respirations. There were a few fine rales heard at both lung bases. The heart sounds were distant, and a slightly split second sound along the left sternal border was heard. The

blood pressure was 160 systolic, and 110 diastolic. The abdomen was hugely obese, rather tense, and flat in most of the dependent portions, with a questionable shifting dullness and fluid wave. There was pitting edema of the feet and lower legs.

The temperature, pulse and respirations were normal.

The urine was clear and acid, with a specific gravity of 1.016 to 1.026, there was a trace of albumin, the sediment showed extremely rare white blood cells, no red blood cells, rare granular casts and, on one occasion, many hyaline casts per high power field. The blood showed a red-cell count of 5,760,000 with 95 per cent hemoglobin, and a white cell count of 7800 with 64 per cent polymorphonuclears. The stools were guaiac negative. The serum nonprotein nitrogen was 30 mg per 100 cc., and the serum protein 6.18 gm., the chlorides were equivalent to 107 cc of N/10 sodium chloride. A phenolsulfonephthalein test revealed an excretion of 55 per cent in one hour. The vital capacity was 1600 cc. An electrocardiogram showed normal rhythm at the rate of 85, interrupted by ectopic ventricular beats. The PR interval was 0.19 second, there was slight slurring of the QRS complexes, a very slightly inverted T_1 , a low T_2 and an upright T_3 .

An x-ray film showed a "large, decompensated heart."

The patient was placed on a Karel diet, with digitalis and bed rest. It was noted that on occasions Cheyne-Stokes respirations occurred, during which time he became cyanotic. He improved rapidly with this regime, however, on the fourth hospital day the peripheral edema had disappeared and on the ninth hospital day he was allowed to be up. His vital capacity was 2650 cc. He was discharged on the fifteenth hospital day with a 1200 caloric diet and $1\frac{1}{2}$ gr of digitalis daily. He had lost from 15 to 20 pounds during his hospital stay. The urine sediment contained no casts when the patient was discharged.

Second Admission (three and a half years later) The patient was followed in the Out Patient Department at regular intervals. He was able to work six days a week and used only two pillows a night for sleep. His weight remained around 204 pounds, and his blood pressure 160 to 180 systolic, 90 to 110 diastolic. At one time he ceased taking digitalis and promptly developed peripheral edema, which was relieved when he again returned to the daily use of the drug. Two weeks before admission the patient caught cold, developed cough and noted an increase in dyspnea and orthopnea and the presence of ankle edema. He complained of

moderate frontal headaches, insomnia and an inability to work.

Physical examination revealed an obese, dyspneic, orthopneic man who appeared older than his years. Cheyne-Stokes respirations were present, and the breath had a urinous odor. Examination of the fundi revealed five tortuous vessels with several small hemorrhages. The disks were pink, slightly blurred but without elevation. The neck veins were distended. The heart was enlarged to the left, with the apex in the anterior axillary line. The rhythm was irregular, with frequent extrasystoles. The pulmonary second sound was exaggerated. There were no murmurs. The lungs were clear except for the presence of a few basal rales. The liver was felt five fingerbreadths below the costal margin and was slightly tender. There was no peripheral edema. The left inguinal ring was large and lax.

Laboratory examinations revealed a negative blood Hinton test, a serum nonprotein nitrogen of 37 mg per 100 cc., a phenolsulfonephthalein excretion of 42 per cent in one hour and a hematocrit of 54. An electrocardiogram showed an inversion of T_1 with a low T_+ , a PR interval of 0.18 second, a ventricular rate of 90 and an auricular rate of 90, with normal rhythm, the QRS complexes in Leads 1, 2 and 3 were slightly slurred.

Final Admission (five months later) With restricted activity the patient did fairly well for a few months following the second discharge. However, starting about two months before the present admission he had had to spend most of his time in bed, and two weeks before admission he became bedridden. He had noted a slight weight loss and complained of increasing dyspnea with the slightest exertion, and orthopnea so that he had to sleep sitting straight up. He had experienced no acute infection, cough or sputum, nor had he noted pain in the chest, ankle edema or swelling of the abdomen.

Physical examination revealed a markedly orthopneic, obese man sitting upright in bed and breathing rapidly. The lips were cyanotic. There was slight sacral edema. The heart was much enlarged to the left, and the pulmonary second sound was accentuated. Occasionally the rhythm was regular at the wrist, and then again it was trigeminal or bigeminal. The liver was felt five fingerbreadths below the costal margin and was slightly tender.

The urine was negative except for a ++++ albumin. The blood was normal. Stools were guaiac negative. An electrocardiogram revealed a ventricular rate of 95 with multiple ventricular premature beats. The PR interval was 0.18 second, the QRS duration 0.10 second, T_1 , T_2 and T_3 were

low, and T_4 slightly high, there was a notched QRS complex, with low voltage, in Leads 1, 2 and 3.

His disease ran a rather hectic course. The temperature ranged from 97°F on admission to from 99 to 102°F in a septic crisis until the time of death. The pulse was around 60, with respirations 25 to 30. He developed dullness at the left base and marked pain in the right lower anterior chest, with Cheyne-Stokes respirations. He became markedly cyanotic, was placed in an oxygen tent but after twelve hours of extreme respiratory embarrassment expired on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. HOWARD B. SPRAGUE This story and these physical findings do not fit in very well with our ordinary categories of heart disease. I do not know whether I can even talk myself into a diagnosis.

Let us review some of the evidence. The man was middle-aged and very obese, having gained 80 pounds in a few years, and he went through three periods of congestive failure but survived for four and a half years after the beginning of his cardiac symptoms. His first complaint was that of orthopnea and then of severe dyspnea on exertion, followed by evidence of peripheral failure with the development of liver enlargement and edema.

The physical findings are not very helpful. He obviously had a big heart, confirmed by the x-ray report of a large decompensated heart with no characteristic shape. There were no murmurs. The pulmonary second sound was accentuated, presumable evidence of pulmonary hypertension but he had none of the other things like gallop rhythm that we might look for in this picture and his blood pressure was borderline (160 systolic, 100 diastolic) when he was first seen. The electrocardiogram does not help very much. He was having cardiac failure with essentially normal rhythm, not auricular fibrillation which would fit in better with some diagnoses than with others. There was only a slight slurring of the QRS complexes, and what changes there were in the T waves might well have been due to digitalis. This first electrocardiogram shows slight inversion of the T waves. In the first lead it looks like a coronary T wave. In the second tracing there is a rather prominent S wave in the first lead but in the chest lead there is a Q wave of 4 mm., which is normal and a normal inverted T wave according to the old technic, essentially the same as the first tracing except that the slight inversion of the T wave in the first lead is less obvious than it was. In the final tracing there is again a slight late inversion of T_1 with low T waves in Leads 2

and 3, but the chest lead is normal and the tracing actually shows less inversion of T_1 than before but a very irritable heart with runs of ventricular premature beats almost like ventricular paroxysmal tachycardia, the thing one observes in terminal toxic conditions. The electrocardiographic evidence, therefore, is inconclusive. It does not hang together in the first and fourth leads as we should like for a diagnosis of coronary occlusion.

He did improve with the ordinary treatment of rest, digitalis and Karell diet and was able to go back to more active work for three and a half years, but he was apparently at the edge of congestive difficulties, because when he stopped taking digitalis the edema recurred and he responded when it was resumed. Because of the story of cold and cough, this second upset seems to have been in relation to a respiratory infection. On the second admission we do have the added evidence that examination of the fundi showed small tortuous vessels with hemorrhages, but the rest of the examination does not help us very much. He again recovered to the point of some activity until the last admission, when he became bedridden two weeks before he came into the hospital. He had no ankle edema or swelling of the abdomen, but marked dyspnea on exertion and orthopnea so that he had to sleep sitting up. At the time of this final admission he was running a temperature and the physical findings would seem to indicate, in addition to some congestive basal rales, that he probably had pulmonary infarction.

In our ordinary groups of hypertension, arteriosclerosis, syphilis and rheumatic fever, where does this fellow fit? He had no evidence of valvular disease, and we can rule out rheumatic heart disease unless we assume some very rare purely myocardial process on a rheumatic basis. There is nothing suggestive of ordinary syphilitic heart disease with involvement of the aortic valve, and he had a negative Hinton test. It may be that some people develop big hearts on the basis of syphilitic myocarditis, but we should like to have more evidence before making that diagnosis. He was forty-six years old. When the trouble started he showed a questionable slight inversion of the T waves in the first lead. Could this represent a coronary occlusion followed by a slowly progressive failure due to the effect of an infarct? There is very little evidence for such a hypothesis. He never had anginal pain, never had an acute attack. It is perhaps of some interest to speculate whether his work as a solderer with lead had anything to do with the development of early arterial change. Or, again, the obesity may have had something to do with it. There is no suggestion

that the obesity was due to myxedema. He was made no better and perhaps worse by the doses of thyroid extract.

Then we have finally the question of hypertension. The big left ventricle was the outstanding thing on physical examination, with a blood pressure ranging up to 180 systolic, 110 diastolic, and evidence of changes of a rather high degree in the retinal arteries but without axis deviation in the electrocardiogram. The electrical axis was entirely normal, and he developed a true low-voltage curve only during the terminal stages of the disease, so that is out of line with hypertensive heart disease.

Then we think of other less obvious diagnoses. Is there anything to suggest that he had trouble predominantly in his right heart—pulmonary hypertension? Did that arise from primary disease in the lungs of an arteriosclerotic nature or from multiple pulmonary emboli with small infarcts and a secondary cor pulmonale? His first symptom was orthopnea without marked physical signs. There is no history of chronic cough, and the physical findings point to left-sided rather than right-sided enlargement, furthermore, there is no real right-axis deviation. There is no evidence of pericardial disease that I can make out. It is not the picture of constrictive pericarditis. There is nothing in the background to suggest that out of a clear sky at the age of forty-six he had succumbed to pericardial disease which must have arisen in childhood, because such a condition is probably always associated with valvular lesions. He may have had an active process in his myocardium or endocardium, or both, at the time of death. At least something was present to account for the fever, and I think pulmonary infarction is the most likely explanation. So I cannot see that we can fit this to any of the categories. We may be dealing with unexplained cardiac enlargement, of which we have seen several cases and which we are unable to relate to rheumatic heart disease, syphilis, toxic foci, a localized myocarditis or anything to which so far we have given a name. It is rather out of line in that connection because these patients usually go downhill rapidly and do not come out of their first attacks to succumb later on.

DR CASTLEMAN: Do these patients have hypertension?

DR SPRAGUE: No, but I think that I shall have to guess that hypertension is the most likely background for the cardiac enlargement in this case. There may be more coronary disease than I suspect, and if not, the enlargement may be of an unexplained etiologic type.

DR PAUL D WHITE: There is one helpful point

in the history that would support Dr Sprague's final belief that hypertension was an important factor the eyegrounds showed considerable arteriosclerosis. Moreover, in the outpatient records it was noted that when his heart failure had cleared after the second stay in the hospital his pressure was 240 systolic, 140 diastolic, and at other times 200 systolic, 115 diastolic. When he appeared in the wards with failure, the blood pressure was consistently lower. That is a significant point. Sometimes blood pressure is high in heart failure when there is a large amount of renal congestion with renal insufficiency but it clears up and drops to normal after the relief of the congestive failure. Sometimes it is the reverse, with the blood pressure dropping toward a "normal level" in heart failure. A blood pressure of 240 systolic, 140 diastolic, was apparently this patient's normal level. I wonder what induced the first failure which came on without coronary symptoms. The story is that of shortness of breath and nocturnal orthopnea which certainly means left ventricular failure. Whether that was the first manifestation or whether, if we had asked him in a little more detail he might have admitted discomfort subternally on effort, we cannot say. One can obtain such a history in most patients with coronary disease. Dr Samuel A. Levine has stated, and I quite agree with him that the more one gets careful histories in cases of suspected coronary disease the more one finds the story of subternal discomfort that may at first have been called breathlessness by the patient.

Another point of importance in this case is that the late inversion of the T waves in Lead 1 is strongly suggestive of the diagnosis of coronary disease. Inversion of T₁ with left axis deviation is frequently found in hypertension alone, but that does not appear quite as does this T wave. Here we find a very late T₁ inversion, the later the inversion of T₁ the more significant it is of coronary disease.

DR. SPRAGUE It looks much more like that than it does inversion due to digitalis or left axis deviation.

DR. WHITE Yes. It is late and strongly suggests coronary insufficiency which may or may not be associated with angina pectoris. It may be due to unrecognized coronary thrombosis. At any rate it does mean coronary insufficiency whether or not there are symptoms thereof. Also the more congestive failure there is, the less clear is coronary disease symptomatically. There is an old rule the more heart failure with coronary disease, the less angina pectoris the more angina pectoris, the less myocardial failure at least for the time being. Coronary thrombosis may, how-

ever, occur suddenly with marked congestive failure, thus accounting for fever.

Another point that I should like to bring up is that when I saw this patient on one occasion at the end of his second hospital entry, when he was convalescing, I thought that he did have chronic hypertensive and coronary heart disease plus respiratory infection which had precipitated myocardial failure. This diagnosis was based on the presence of a large heart plus a hypertension which had been at times more than it was found to be in the ward and on the coronary type of electrocardiogram, plus the fact that a middle aged or older man with hypertensive heart disease is likely to have coronary disease. A large heart with congestive failure does not need to produce inversion of the T waves in Lead 1.

The only remaining question concerns the heart failure, which was first due to left ventricular strain and then became a total heart failure. Why should he have recovered from his first failure and been relatively well for two or three years? I expect one answer is that he reduced his weight 50 pounds or more in that interval. Weight reduction is a very important method of treatment of this condition when, as here, there is great obesity. In conclusion, I think Dr Castleman will find that this patient had hypertensive and coronary heart disease, with heart failure and possibly terminal pulmonary embolism.

A PHYSICIAN It strikes me that the initial failure may have been due to thrombosis in a silent area of the heart.

DR. WHITE He might certainly have had coronary thrombosis, although the story is not characteristic. Digitalis, which he took in the dose of three pills a day, he continued for a long time—six months. He was a big man and able to take a lot of digitalis. Even so it seems a big dose, if each pill contained 1½ gr. Of course, he had some rest therapy as well as digitalis.

DR. CASTLEMAN I spoke to this man's family physician who informed me that he was very difficult to treat because he insisted on working. I believe that while he was getting the digitalis he did a little work on the side and did not get the rest he should have had.

A PHYSICIAN What are the other causes of hemorrhages in the eyegrounds?

DR. WHITE No other causes such as serious renal disease or cerebral or ophthalmic lesions were apparent in this case. Hypertension was by far the most obvious cause.

CLINICAL DIAGNOSES

Essential hypertension.

Hypertensive and arteriosclerotic coronary heart disease, with congestive failure.

Pulmonary infarct
 ? Bronchopneumonia

DR HOWARD B SPRAGUE'S DIAGNOSES

Hypertensive heart disease
 Coronary sclerosis
 Terminal pulmonary infarction

PATHOLOGICAL DIAGNOSES

Cardiac hypertrophy, hypertensive type
 Pulmonary infarction, multiple
 Arteriosclerosis, marked, coronary, aortic and cerebral
 Pulmonary congestion
 Infarcts of kidney and spleen, old
 Thrombosis of popliteal vein, right

PATHOLOGICAL DISCUSSION

DR CASTLEMAN The autopsy showed a very large heart, weighing 780 gm. There was hypertrophy of both the right and left ventricles, the right ventricle measuring 8 mm., which is a little more than twice normal. Since there were no valvular lesions one certainly would consider it a true hypertensive heart. The coronaries were markedly sclerotic and calcified. In several places only pinpoint lumens could be seen, but there was no evidence of thrombosis or myocardial infarction. Microscopically only the slightest amount of fibrosis was found throughout the myocardium, such as is almost always seen with coronary disease. He showed all the signs of heart failure. There were 500 cc of fluid in the right pleural cavity, 100 cc on the left. The lungs were markedly congested. In addition, there were about a dozen infarcts throughout all lobes of the right lung and two in the left lower lobe. Some of the infarcts were fairly old and probably account somewhat for the hypertrophy of the right heart. I am sure he had some on his previous admission. The source of the emboli was the right popliteal vein, where a large thrombus was found.

DR WHITE Was there any indication clinically that he had phlebitis?

DR CASTLEMAN No.

He also had evidence of embolism in the systemic circulation. There was an old infarct in one kidney and another in the spleen so that we may assume that during some of the hospital admissions he had had a mural thrombus in the left auricular appendage which had broken off. We found no evidence of it, however, at autopsy.

DR WHITE He may have started the illness with pulmonary embolism causing dyspnea, and following that congestive heart failure.

DR CASTLEMAN I think it is more likely that

failure began as a consequence of his coronary disease.

DR WHITE He might have had the combination plus hypertension.

DR CASTLEMAN He had severe arteriosclerosis throughout the body, especially marked in the brain, but we were unable to find any softening.

DR SPRAGUE Do you know whether he had a bad family history or whether lead had anything to do with the picture?

DR CASTLEMAN I believe he did have a family history of hypertension.

A PHYSICIAN Any nephrosclerosis?

DR CASTLEMAN Very slight. He certainly did not die of kidney failure.

DR WHITE He really represents hypertensive heart disease so far as the myocardium is concerned except that the extensive coronary disease added its quota of insufficiency to precipitate myocardial failure. I think he would have eventually shown congestive failure even without the coronary disease. The hypertensive effect was on both ventricles, first on the left and then, secondarily, on the right. Finally both ventricles failed.

DR CASTLEMAN A postmortem film shows fluid and bilateral infarcts.

DR WHITE If anything, we are overdiagnosing pulmonary infarcts now because we have found so many pulmonary infarcts complicating congestive failure. They are almost always multiple rather than single.

CASE 25442

PRESENTATION OF CASE

A fifty-three-year-old carpenter was admitted to the hospital complaining of shortness of breath for three months.

The patient was apparently well until about one year before entry when he noted a constant "tiredness" on awakening mornings, this forced him to sit and rest on the side of the bed before getting up. About six months before entry the patient contracted a "cold" characterized by general malaise, poor appetite and further "tired" feelings. There was no known fever. About two weeks later he began to have dyspnea on slight exertion. He spent two weeks in an outside hospital and improved with digitalis therapy. After discharge he continued to take digitalis, three pills a day, and was followed by his doctor for six weeks, at the end of which time he discontinued the medications because he saw "no benefit from the medicine." He continued to work as a carpenter until one month before entry when he again noticed increasing dyspnea, early orthopnea and insomnia and experienced regular attacks of

asthmatic gasping breathing at about three o'clock every morning. Two weeks before entry ankle edema had appeared. All these symptoms increased until ten days before admission when he became dyspneic even on sitting quietly. He was then given "quinidine, six tablets per day for the irregular heart, but this apparently caused nausea, vomiting and malaise, with an associated increase in edema after a week's use of the drug. He had had "scarlet fever" at the age of seven. Otherwise the family, marital and past histories were noncontributory.

Physical examination revealed a well-developed and poorly nourished man in definite respiratory distress, with Cheyne-Stokes breathing. The arteries of the fundi were thin and showed marked nicking. The neck veins were distended. The chest was barrel shaped. The heart was markedly enlarged to the left, and the rate was regular with occasional extrasystoles. There were continuous blowing systolic and diastolic murmurs at the apex which replaced the heart sounds. A distinctly rough systolic murmur at the aortic area was transmitted to the neck but was unaccompanied by a thrill. The aortic second sound was markedly diminished and was less than the pulmonary second sound. The blood pressure was 90 systolic, 60 diastolic. The lower half of both lung fields posteriorly and laterally were dull to percussion, and the breath and voice sounds were decreased to absent, with medium to fine moist rales. The liver edge was tender and was palpated two and a half fingerbreadths below the costal margin. There was pitting edema of the feet and lower legs. The remainder of the examination was negative.

The temperature was 97.6°F., the pulse 80 and the respirations 20.

Examination of the blood revealed a red-cell count of 4,600,000 with 85 per cent hemoglobin and a white-cell count of 10,700 with 78 per cent polymorphonuclears. The blood serum nonprotein nitrogen was 66 mg. per 100 cc. An electrocardiogram showed a ventricular and auricular rate of 80 per minute, with ventricular premature beats, a PR interval of 0.18 second and a QRS duration of 0.13 second, the QRS complex was slurred, and there was a right bundle branch block. A blood Hinton test was negative. X-ray examination of the chest revealed a heart markedly enlarged to the left with an elongated aorta and prominent aortic knob without evidence of dilatation. The hilar vessels were increased in size. There was a small amount of fluid in the left pleural cavity.

The patient on admission was in obvious distress with orthopnea, Cheyne-Stokes respirations, an enlarged liver and peripheral edema. He was placed on a cardiac regime, including digitalis,

Salyrgan, aminophyllin, morphine and complete bed rest. He improved quickly but not dramatically and was allowed out of bed on the fourteenth to eighteenth hospital days. He tired easily and began to show Cheyne-Stokes respirations again, he was then put back on complete bed rest and digitalis. On the twenty-ninth hospital day an electrocardiogram showed persistent right bundle-branch block with ventricular premature beats. He continued to become slowly but steadily more dyspneic. During the fifth week he became worse, with increased dyspnea and pains in the low back and in the "bones of the legs." The temperature rose to 101°F., the pulse to 100 and the respirations to 24. He developed a marked systolic thrill and harsh murmur over the aortic area, with dullness and increased breath sounds and fremitus in the right chest anteriorly. An electrocardiogram showed persistent bundle branch block with numerous premature beats arising in both auricles and ventricles. Digitalis was discontinued. On the forty-third day he went into circulatory collapse, developing cold, pulseless extremities and cyanosis, and died.

DIFFERENTIAL DIAGNOSIS

DR. C. EDWARD LEACH: The description indicates a present illness relatively free of complicating factors. It seems one primarily of cardiac insufficiency, progressive in degree, beginning with left ventricular failure as evidenced by dyspnea, at first associated with exertion and relieved by rest and digitalis in the hospital. However, a short time later the same symptoms though of greater severity, recurred, perhaps returning more rapidly because he had discontinued digitalis. Subsequently he developed frequent attacks of probable cardiac asthma with increasing orthopnea and dyspnea and three months before entry ankle edema indicated right ventricular failure.

The physical examination showed practically all the signs of advanced heart failure, with evidence of pulmonary congestion as well as congestion of the systemic circulation. The heart itself revealed marked enlargement, chiefly to the left. The rough systolic murmur described in the aortic area and transmitted to the neck, together with the blood pressure and diminished aortic second sound makes a fairly characteristic picture of aortic stenosis. The apical murmurs were not quite so clear cut. The diastolic murmur at the apex, which was described as blowing in character, is confusing. An aortic diastolic murmur may be heard at the apex and have a blowing quality. I have never heard a mitral diastolic murmur that was not rumbling. No basal diastolic murmur is described and I must therefore assume that this was not a transmitted murmur. At the

apex even functional diastolic murmurs have a rumbling quality, and I wonder whether this description of the apical signs might err a bit in either the timing or quality of the murmurs. It does not suggest to me organic mitral-valve disease, and it is more likely that the murmurs at the apex were functional, perhaps associated with dilatation of the left ventricle.

At the time of entry to the hospital there was no evidence of complicating factors other than heart disease and heart failure. The temperature was normal. The blood counts at that time, the white count particularly, were not remarkable. The nonprotein nitrogen of 66 mg per 100 cc might go with a fairly severe congestive failure, and it is unnecessary to introduce primary renal disease to explain it. It seems to me that aortic stenosis was the important cardiac lesion. The intensity of signs and the age of the patient favor the calcareous type. There is a note that he had had scarlet fever at the age of seven, which introduces a possible etiologic factor for pre-existing valvular disease. This may have been rheumatic fever. Many of the cases of calcareous aortic disease that we see have a history suggesting rheumatic fever in the past, but often this is lacking. The most significant thing in the electrocardiogram is the evidence of right bundle-branch block. I think this probably indicates coronary disease in addition to the aortic valvular disease, since coronary disease is by far the most frequent cause of bundle-branch block and it is not usually found in valvular heart disease.

His early hospital course, during which he apparently improved under treatment, was presumably uncomplicated. He was apparently doing well and was allowed up for a few days. Then he became worse and at that time there were probably some complicating factors in his illness. According to the record he became slowly but steadily more dyspneic, and during the fifth week of his stay he had a recurrence of increasing failure. The temperature rose to 101°F, the pulse to 100, and the respirations to 24. Associated with this he apparently had a change in the character of the murmur at the aortic area, and a systolic thrill was felt at that time. He also complained of pains in the lower back and in the bones of the legs. There is no note as to how long this temperature elevation persisted or whether it was present up to the end of the illness, but in conjunction with the change in the murmur, one is forced to think of a bacterial endocarditis superimposed on the valvular disease. However, that would be a rather unlikely occurrence in a calcareous type of valvular involvement. There is an additional note that he had evidence of pulmonary consolidation at that time, a better ex-

planation of the fever. He went rather rapidly downhill up to the time of the terminal episode. The increasing number of premature beats indicates a greater irritability of the heart associated with increasing heart disease and heart failure or overdigitalization. Digitalis was stopped, probably because of the latter possibility.

His terminal episode was one of circulatory collapse and as described here gives little clue to the responsible factor. Coronary occlusion, pulmonary infarction, cerebral accident or even ventricular fibrillation would fit the description that is given. However, no particular mention of pain is made, which we might expect in coronary thrombosis, and no obvious signs of cerebral accident are described. With the pulmonary signs previously noted at the onset of fever it seems likely that pulmonary infarction is a reasonable explanation of the terminal failure and death. A great many patients with marked aortic stenosis die suddenly, and this has been explained by the patient's inability to increase cardiac output, important because of the stenotic orifice that limits the amount of blood ejected. Similarly a sudden strain on the heart by further lowering the output might be incompatible with life. It seems reasonable to me that he had in the last few weeks several pulmonary infarcts and that the terminal episode represented sudden death due to changes in the cardiac output associated with additional pulmonary infarction. I do not see how we can tell whether he had pre-existing rheumatic heart disease, since the description of physical signs does not allow a positive decision regarding mitral disease, and his past history is essentially negative. I think it would be very unlikely that the aortic stenosis was entirely rheumatic since he had had no symptoms until six months or a year before his death. I shall leave open the question of pre-existing rheumatic heart disease and advance for my diagnoses calcareous aortic stenosis, cardiac failure, coronary arteriosclerosis and multiple pulmonary infarcts.

DR EDWARD F BLAND. This man was quite a problem. He was obviously very ill. We called up his doctor to find out about the medicine he had been taking. We were interested in the statement about quinidine, which he had been given outside because his heart had been irregular. It apparently helped the irregularity, but the patient got worse. Digitalis had been tried a short while before, but given up. When he arrived at the hospital he was in severe congestive failure. The physical signs were interpreted at that time as indicating both aortic stenosis and regurgitation. In addition to the basal murmurs he had a moderately loud mitral systolic and loud apical diastolic rumble. We thought the prog-

nosis was poor and that he would not survive the episode. The Cheyne-Stokes respiration was even more troublesome than the orthopnea. He was given vigorous digitalis and diuretic therapy but ultimately failed and died.

Dr. PAUL D. WHITE: I think Dr. Leach is quite justified in believing that the electrocardiographic finding of bundle-branch block suggested coronary disease. We have, however, seen a few instances of calcareous aortic stenosis where the lesion at the base of the aortic valve was very close to where the bundle of His and its branches come through, and impinged on the bundle giving rise to heart block without much of any coronary disease. I believe Dr. Leach is correct in assuming that there was no bacterial endocarditis. It was noted that there developed a thrill. Do you remember it, Dr. Bland?

Dr. BLAND: There was a very well-defined aortic systolic thrill.

Dr. WHITE: It is rare for calcareous aortic stenosis to be complicated by bacterial endocarditis.

Dr. BENJAMIN CASTLEMAN: Unless it is bicuspid I have seen a few such cases in which there was a subacute bacterial endocarditis.

Dr. FRANCIS M. RACKEMANN: One note impresses me. This man had a barrel-shaped chest. The interesting question is whether such a chest can develop relatively suddenly as the result of respiratory disease or whether it in itself indicates long-standing disease of the lungs. In this case, the shape of the chest is well shown by the x-ray film, which demonstrates the very marked bulge of the lower ribs and the flat diaphragm. On the other hand, the barrel-shaped chest indicates that the trouble had been of considerable duration.

According to the history, the onset of symptoms in this case was at the age of fifty-two when the man was apparently in good general health. This onset was mild, and it was six months later, when he caught a new cold that more severe symptoms first appeared.

On several grounds, therefore, it seems proper to assume that the beginning of the heart trouble was some time before the onset of his infection and that one cannot blame the infection for the basic cause of the heart trouble. I should like to ask whether it is not entirely proper to suspect that this man had something wrong with his heart for many years before the apparent onset of his disease.

There is one other small point. Whenever I read the words "asthmatic gasping" I perk up a little and think of some process other than heart disease. On the other hand it is easy to recog-

nize of conditions and that both may occur quite commonly in cases of this kind.

Dr. WHITE: In answering Dr. Rackemann I should say that we all agree that this heart disease was of long standing. The calcareous change, even though it was calcareous change without fundamental preceding rheumatic valvular disease, was doubtless a good many years in developing if there was a rheumatic valvular lesion first. The heart disease dates back probably forty years. This man's barrel chest probably did not arise in a month from his cardiac asthma. I do not know how long it takes to develop a barrel chest. Do you, Dr. Sprague?

Dr. HOWARD B. SPRAGUE: No.

CLINICAL DIAGNOSES

Rheumatic and arteriosclerotic heart disease with mitral and aortic stenosis and regurgitation.
Congestive failure.
Pulmonary infarct.

Dr. LEACH'S DIAGNOSES

Calcareous aortic stenosis.
Cardiac failure.
Coronary arteriosclerosis
Pulmonary infarcts

ANATOMICAL DIAGNOSES

Aortic stenosis, calcareous
Cardiac hypertrophy, hypertensive type.
Endocarditis chronic rheumatic, mitral and aortic, with stenosis.
Pericarditis chronic fibrous, adhesive, localized.
Pulmonary edema
Chronic passive congestion of the liver
Thrombosis, perivesical veins.

PATHOLOGICAL DISCUSSION

Dr. CASTLEMAN: This man had a very large heart, weighing 800 gm., the enlargement being due to marked hypertrophy of the left ventricle produced by a severe degree of calcific aortic stenosis. The valve was very rigid and certainly must have been both stenotic and insufficient. The mitral valve was also involved, showing slight but unquestionable rheumatic changes. There was slight shortening and thickening of the chordae tendineae but without any appreciable stenosis. There were also pericardial adhesions, which are consistent with a rheumatic story. The liver showed marked congestion, and the lungs a large amount of edema and congestion. There was no infection or infarction in the lungs. The coronary arteries showed very slight atheromatous changes and could be considered perfectly normal for his age.

Dr. COX: Did the calcification extend down far?

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
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United States Canada \$7.04 per year \$8.52 per year for all foreign coun-
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MATERIAL for early publication should be received not later than noon
on Saturday

THE JOURNAL does not hold itself responsible for statements made by any
contributor

COMMUNICATIONS should be addressed to the *New England Journal of
Medicine* 8 Fenway Boston Mass

SIGMUND FREUD'S CONTRIBUTIONS TO MEDICINE

FOLLOWING Sigmund Freud's death it is timely to comment on his contributions to medicine, for they have had universal interest both to the profession and to the general public. It was Freud's psychoanalytic writings which have excited the greatest interest, whereas his earlier work in the fields of clinical and comparative neurology is far less known and is infrequently mentioned. In fact, in Freud's collected works, there is no reference to these special contributions, and it is only in his autobiography that Freud briefly described his investigations previous to his notable contributions to psychology, psychiatry and psychoanalysis.

When a young man, Freud worked under Brucke and Meynert, first in comparative neurology

and then in clinical neurology, human cerebral anatomy and neuropathology. It was in July, 1884, that he wrote a short monograph on cocaine, being the first to note its properties as a local anesthetic, in this monograph he prophesied that further uses for the alkaloid would be found. In 1885, on the basis of his histological and clinical publications, he was appointed lecturer on neuropathology at the University of Vienna. In 1897, he contributed the section on infantile cerebral palsies to Nothnagel's *Specielle Pathologie und Therapie*. His most important contributions during this period are the monographs on aphasia, cerebral diplegia and infantile cerebral injuries, work of a high order of originality.

Freud's interest in psychological medicine was stimulated by his work with Charcot in 1885 at the Salpêtrière, where he was impressed with the latter's investigations on hysteria and on the effects of hypnotic suggestion. Later he translated Charcot's lectures on nervous diseases, and also Bernheim's volume on suggestive therapeutics. On his return to Vienna, he soon abandoned the treatment of organic nervous diseases, which he thought at that time offered little of promise, and turned to the field of neurotic disorders.

Freud's earliest works on hysteria date from about the year 1886, and the first fundamental contribution to psychoanalysis, written in collaboration with Breuer and entitled "*Ueber den psychischen Mechanismus hysterischer Phänomene*" ("Psychic Mechanisms of Hysterical Phenomena"), appeared in 1893. At first the therapy of choice was hypnotic suggestion, later the significance of the emotional life of hysterical patients was discovered, and this led to a therapeutic aim without the use of hypnosis, termed "catharsis." Then followed the transition from catharsis to psychoanalysis, with its special and complicated technique based on free associations and the investigation of dream processes.

From then on, Freud was a very prolific writer on the general subject of the mechanism and psychotherapy of the psychoneuroses. These investigations gradually led to his conceptions of the impor-

int part played by unconscious mental processes in the neurotic disorders, and as a result of these discoveries, he began to note the prominent role played by both the sexual and the ego instincts in the personality of both neurotic and normal individuals. These inquiries led, in 1900, to the publication of his monumental volume on the interpretation of dreams. In this book, he demonstrated for the first time the value of understanding dream material and the processes of dream formation for a comprehension of the unconscious setting of psychic disorders. He showed that the real meaning of the dream could not be determined from the dream as remembered, which is termed the manifest content and which was distorted and expressed in symbolic form, but only through the process of free association which led to the web of dream thoughts, that is, the latent content of the dream. It was these dream thoughts which not only illuminated the dream and showed that the fundamental trend of the dream was that of a wish fulfillment but, at the same time, explained through their analysis the neurotic symptoms. It was years later that Freud revised in part his original theory of dreams, with particular reference to the anxiety problem, though keeping the fundamental theory intact.

As time went on, the technic of analysis became more developed, and subsequently Freud published five minutely detailed case histories to illustrate the technical methods utilized in the interpretation and therapy of hysteria, obsessional neuroses and paranoia. In one of these case histories, "*Bruchstück einer Hysterie Analyse*" ("Fragment of an Analysis of a Case of Hysteria"), published in 1905 he discussed in detail the unconscious motives of neurotic illness and also the important phenomenon of "transference, the latter forming the basis of all psychotherapeutic methods although worked through only in analysis.

The extensive contributions of Freud to medicine have comprised a multiplicity of subjects, such as fundamental conceptions on the psychology of sex, the problem of anxiety, the meaning of slips of the tongue, investigations on the structure and functions of the mental apparatus, dynamic concepts of the personality, the psychology of instinctive drives in the psychoneuroses, the problem of repression, and the purely technical aspects of psychoanalysis.

Freud's work on the structure and functions of the mind, published in 1923 and translated into English under the title of *The Ego and the Id* has had a great influence on contemporary descriptive and interpretative psychiatry, particularly the concepts of ego, id and superego, and on the clinical observation of what is termed a "negative therapeutic reaction, that is resistance to recovery from a neurosis produced by an unconscious sense of guilt.

Indeed as Freud's work of half a century is reviewed as a whole, it becomes apparent that psychoanalysis, which began solely as a specific therapeutic method, gradually evolved into a science of unconscious mental processes, a science necessary for the understanding of normal and neurotic reactions and an essential part of the development of modern psychiatry.

THE NATIONAL CANCER INSTITUTE

THE interest of Massachusetts in the rapidly developing National Cancer Program is particularly keen in view of the fact that this state was the first to recognize cancer as a public health problem. The late Drs G. H. Bigelow and R. B. Greenough and the present director of the Division of Cancer of the Massachusetts Department of Public Health, Dr. H. L. Lombard, organized an attack on the disease that, aided by medical men and other public spirited citizens, has led to a better control of cancer than any other state has yet developed, as judged by that ultimate grim standard, the death rate from the disease. The success of this pioneer work in Massachusetts has had no small influence in recognition of the problem of cancer control as a feasible subject for national public-health effort. We can also have pride in the fact that our congresswoman from Lowell, Mrs. Edith Nourse Rogers, was an important factor in the passage of the National Cancer Institute Act.

The new National Cancer Institute, at Bethesda, Maryland, a part of the National Institute of Health, affords a splendid opportunity for continu-

ing and expanding the excellent work that the United States Public Health Service has been carrying on in this field. Unfortunately, in centralizing the anti-cancer forces of the Service, Boston will be deprived of one of its most important groups of cancer investigators. This unit of the United States Public Health Service, which has developed under the lead of Dr J W Schereschewsky and Dr F C Turner, has been carrying on sound and careful investigations for years. Of special importance, the group, in collaboration with Prof L F Fieser, of the Department of Organic Chemistry, Harvard University, has made outstanding contributions to our knowledge of carcinogenic hydrocarbons. In spite of this serious local loss, our hospitals, medical schools and doctors will close ranks and carry on, with high hopes for the work our friends will do in their new quarters.

It should be the pride of every doctor in the State to do his part in cancer education and cancer therapy, for the backbone of the Massachusetts program is the co-operation of the medical profession. Continued progress and increased prestige for this program give further emphasis to the value of community efforts toward better health when guided and controlled by medical men.

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Boston

SEPTIC ABORTION

Mrs V L C, a twenty-six-year-old para II, who was about fourteen weeks pregnant, was sent into the hospital by her private physician on June 28, 1937. The previous day he had attempted to empty the uterus because of active bleeding due to spontaneous abortion. The bleeding was so great that he packed the uterus, having succeeded in removing none of the products of conception.

The family history was negative. The patient had had scarlet fever as a child, and her tonsils

had been removed. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted five days. Her last period had begun the middle of March. Her previous pregnancy had been normal throughout and had terminated normally in July, 1936.

Physical examination on entrance showed a well developed and nourished young woman. The heart was not enlarged, there were no murmurs. The lungs were clear and resonant, there were no rales. The temperature and pulse were normal. The uterus was enlarged consistent with her dates and was palpable above the symphysis. Vaginal examination showed the cervix filled with gauze.

On June 29, the day following entrance, the pack was removed. She began to bleed very freely. The uterus was explored, and the amniotic sac was broken with the escape of a large amount of fluid. The fetus except for the head was removed, together with a large amount of placental tissue. The uterus was packed with an iodine strip, not because of bleeding but because it was appreciated that the uterus was not empty and that it was necessary to stimulate uterine contractions. This was removed the following day. The temperature on July 1 and 2 ranged from 98.6 to 102°F. There was no further bleeding. The fetal head was passed spontaneously, but remnants of placental tissue were still retained. The temperature on July 3 ranged between 99 and 100°F. On July 4, following a chill, the temperature rose to 104°F, and the pulse to 124. The following day the temperature gradually came down to 99°F, but the pulse remained elevated from 100 to 120. On July 6 the temperature was normal, but flowing increased.

On July 8 she bled rather freely for about an hour, she also had a slight chill with the temperature rising to 103°F, and the pulse to 130. Because of continued bleeding and in spite of the chill, it was considered necessary to invade the uterus in an attempt to remove the adherent placental tissue which was causing the hemorrhage. The uterus was explored manually and a large amount of adherent placental tissue was removed. The uterus was again packed with an iodine strip, which was removed later in the day. On July 10 the temperature was normal, and the pulse about 100, there was no more flowing. From then on the temperature remained constantly at a normal level and the pulse gradually came down to 80. She was discharged on July 22.

The following blood work was done: June 29, hemoglobin 92 per cent, red-cell count 4,500,000, white-cell count 7700, July 4, white-cell count 8750, July 6, hemoglobin 57 per cent, red-cell count 2,950,000, July 7, hemoglobin 52 per cent, red

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

cell count 2,830,000, July 9 hemoglobin 40 per cent, red-cell count 2,300,000, white-cell count 8600, July 12, hemoglobin 39 per cent, red-cell count 2,300,000, July 14, hemoglobin 43 per cent, red-cell count 2,350,000, July 16, hemoglobin 46 per cent, red-cell count 2,300,000 July 19, hemoglobin 59 per cent, red-cell count 3,500,000, July 22, hemoglobin 69 per cent, red-cell count 3,400,000, white-cell count 8850

A blood culture taken on July 4 showed no growth. A culture from the vagina on July 6 showed staphylococci, and a culture from the uterus on July 8 showed anaerobic staphylococci and anaerobic gram-negative bacilli. On June 29 the pathologist reported "placental tissue and fetus," and on July 8 placental tissue, necrosis, masses of bacteria."

Comment This case illustrates the unhappy course of some spontaneous abortions that occur between the twelfth and fourteenth weeks of pregnancy. A great deal of bleeding sometimes occurs before the cervix is open sufficiently to remove the fetus and the placenta. As in this case, instrumental dilatation results in such profuse hemorrhage that the uterus cannot be emptied and packing is the only safe procedure. Packing of the cervix in cases of bleeding in spontaneous abortion at this stage of pregnancy is done for the purpose of controlling hemorrhage and of softening the cervix, with the hope that when the pack is removed the uterus will empty itself without further complication. This case illustrates the fact that such a result does not always follow since the uterus had to be packed once more after a good part of the products had been removed manually. In spite of the septic temperature, con- servatism was followed. It was known that the uterus was not empty, but until hemorrhage made intrauterine manipulation necessary the uterus was left alone. The third operation was carried out with extreme care, the fingers alone being used so that the possibility of spreading the infection was reduced to a minimum. This emphasizes the great need of following the general principle that hemorrhage is the only indication for entering an infected uterus.

The question of transfusion when the hemoglobin had reached 40 per cent and the red-cell count 2,300,000 was entertained, but since there was no more hemorrhage, it was believed that iron medication, diet, sunlight and fresh air would suffice.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning November 6

BARNSTABLE

Sunday November 12 at 4 00 p.m., at the Cape Cod Hospital, Hyannis. Gonorrhea in the Female. Instructor Oscar F. Cox, Jr. Donald E. Higgins, *Chairman*

BRIXTOL NORTH

Thursday November 9 at 4 00 p.m. at the Morton Hospital, Taunton. Indications for Cesarean Section. Instructor Judson A. Smith. Lester E. Butler, *Chairman*.

BRIXTOL SOUTH (New Bedford Section)

Friday November 10 at 4 00 p.m. at St. Luke's Hospital, New Bedford. Pneumonia. Instructor Charles A. Jancway. Robert H. Goodwin, *Chairman*

ESSEX NORTH

Friday November 10 at 4 30 p.m., at the Lawrence General Hospital, Lawrence. Cardiovascular Disease. Eleven important questions about heart disease and their answers. Instructor Edward F. Bland. John Parr, *Chairman*

ESSEX SOUTH

Tuesday November 7 at 4 00 p.m., in the Conference Room of the Salem Hospital, Salem. Gonorrhea in the Female. Instructor P. N. Papas. J. Robert Shaughnessy, *Chairman*

MIDDLESEX EAST

Tuesday November 7 at 4 00 p.m., at the Melrose Hospital, Melrose. Convulsions in Infants and Children—Etiology and Treatment. Instructor Charles F. McKhann. Walter H. Flanders, *Chairman*

MIDDLESEX NORTH

Friday November 10 at 4 45 p.m., at St. John's Hospital, Lowell. Common Problems of Neurology—Indications for lumbar puncture. Instructor T. J. C. von Storch. William S. Lawler, *Chairman*

WORCESTER (Milford Section)

Tuesday November 7 at 8 30 p.m., in the Nurses Home of the Milford Hospital, Milford. Syphilis in Pregnancy and the Offspring. Instructor William P. Boardman. Joseph Ashkins, *Chairman*

WORCESTER (Worcester Section)

Friday November 10 at 8 00 p.m., in the Staff Room of the Worcester City Hospital, Worcester. Head and Spine Injuries. Instructor Donald Munro. George C. Tully, *Chairman*

WORCESTER NORTH

Friday November 10 at 4 30 p.m., in the Nurses Home of the Burbank Hospital, Fitchburg. Common Laboratory Procedures in Pediatrics and Their Interpretation. Instructor John A. V. Davies. George P. Keaveny, *Chairman*.

DEATHS

CHESLEY—ALFRED E. CHESLEY, M.D., of Lawrence, died recently. He was in his sixty-fourth year.

Born in North Andover, he attended Dartmouth College and received his degree from New York University College of Medicine in 1904. For thirty years he had been a member of the senior medical staff of the Lawrence General Hospital. He was a member of the Massachusetts

Medical Society, the New England Otological and Laryngological Society, and the Lawrence and Essex County medical societies. Dr Chesley was also a fellow of the American Medical Association.

His widow, a son and a daughter survive him.

MUNRO—WALTER L. MUNRO, M.D., of Providence, Rhode Island, died October 23. He was in his eighty third year.

Dr Munro received his degree from Harvard Medical School in 1885, and practiced in Meriden, Connecticut, before going to Providence. He was consulting surgeon for the principal hospitals of Providence and Pawtucket and was a retired fellow of the Massachusetts Medical Society. He also held fellowships in the American Medical Association and the American College of Surgeons.

A sister, a daughter, Dr Rose C. Munro, a son and a nephew survive him.

SPARHAWK—CLEMENT W. SPARHAWK, M.D., of Salem, died October 22. He was in his eighty sixth year.

He was born at Para, Brazil, but received his education in Boston and attended Harvard University. In 1884 he received his degree from the Harvard Medical School and served internships at the Carney and Boston City hospitals.

Dr Sparhawk first opened his office in West Roxbury. Later he practiced in Plymouth and from there moved to Danvers. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a brother and three nieces survive him.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1939

DISEASES	SEPTEMBER 1939	SEPTEMBER 1938	FIVE YEAR AVERAGE*
Anterior poliomyelitis	20	4	139
Chickenpox	87	82	85
Diphtheria	16	8	19
Dog bite	925	819	829
Dysentery, bacillary	56	29	18
German measles	20	18	27
Gonorrhea	419	529	543
Lobar pneumonia	82	120	114
Measles	78	138	76
Meningococcus meningitis	2	5	4
Mumps	57	144	143
Paratyphoid B fever	6	16	9
Scarlet fever	99	139	197
Syphilis	335	516	431
Tuberculosis, pulmonary	215	232	248
Tuberculosis, other forms	24	35	28
Typhoid fever	9	2	16
Undulant fever	1	1	2
Whooping cough	401	375	447

*Based on figures for preceding five years.

RARE DISEASES

Actinomycosis was reported from Everett, 1, Revere, 1, total, 2.

Anterior poliomyelitis was reported from Amherst, 1, Boston, 4, Dartmouth, 1, Fall River, 1, Franklin, 1, Malden, 1, Melrose, 1, New Bedford, 1, Newton, 2, Quincy, 2, Revere, 1, Waltham, 1, Watertown, 1, Wellesley, 1, West Brookfield, 1, total, 20.

Diphtheria was reported from Boston, 1, Brookfield, 1, Cambridge, 3, Fall River, 3, Lawrence, 2, Merrimac, 1, Methuen, 1, Salem, 1, Worcester, 3, total, 16.

Dysentery, bacillary, was reported from Boston, 1, Danvers, 2, Lowell, 2, Revere, 1, Warcham, 1, Worcester, 3, Wrentham, 46, total, 56.

Infectious encephalitis was reported from Malden, 1, total, 1.

Malaria was reported from Chelsea, 1, Foxboro, 1 (therapeutic), total, 3.

Meningococcus meningitis was reported from Lawrence, 1, Lowell, 1, total, 2.

Paratyphoid B fever was reported from Boston, 1, Brookline, 1, Chelsea, 1, Fall River, 1, Greenfield, 1, Newton, 1, total, 6.

Pellagra was reported from Boston, 1, Westfield, 1, total, 2.

Septic sore throat was reported from Boston, 2, Fall River, 1, total, 3.

Tetanus was reported from Longmeadow, 1, Milford, 1, total, 2.

Trachoma was reported from Boston, 1, Lynn, 1, total, 2.

Tularemia was reported from Boston, 1, total, 1.

Typhoid fever was reported from Boston, 1, Douglas, 1, Fitchburg, 2, Haverhill, 1, Ipswich, 1, Lawrence, 1, New Bedford, 1, Springfield, 1, total, 9.

Undulant fever was reported from Ware, 1, total, 1.

Scarlet fever and typhoid fever had their lowest reported September incidence.

Lobar pneumonia was reported at its lowest level since 1933.

The reported incidence of anterior poliomyelitis and meningococcus meningitis was within normal limits.

Bacillary dysentery was reported at a higher level than usual.

Diphtheria, paratyphoid B, and whooping cough remained within the five-year average.

Chickenpox, German measles, and measles showed nothing unusual.

Tuberculosis, pulmonary and other forms, remained at a consistently low figure.

Mumps and undulant fever were reported at a very low level.

NOTES

Dr. Walter B. Cannon, professor of physiology at the Harvard Medical School and president of the American Association for the Advancement of Science, recently delivered a series of lectures at the University of North Dakota under the sponsorship of the Society of Sigma Xi, the Graduate Club, the University of North Dakota School of Medicine and the district medical society. The titles were "Maintenance of Stable States in the Body," "Chemical Mediation of Nerve Impulses" and "Effects of Strong Emotions."

Dr. Aldo Luisada has recently been appointed to a full-time associate professorship in the faculty of Middlesex University School of Medicine. Dr. Luisada received an M.D. degree in 1924 from the University of Florence, then worked in the clinics of Professor Vaquez, of Paris, Professor Loewi, of Graz, and Professor Pick, of Vienna. He then became assistant in the medical clinic of Professor Frugoni in Padua, where he had the direction of an experimental laboratory for physiological and pharmacological research. He served as professor of internal medicine and director of the institute for special pathology at the University of Sassari, and later in the same capacity at the University of Ferrara.

CORRESPONDENCE

ASH INDEMNITY PAYMENTS

To the Editor The other day in perusing the July 27 issue of the *Journal* I ran across an editorial which suggested that cash indemnity was now playing a very large part—and apparently a very valuable part—in the solution of the problem of the cost of medical care. You were used an expression which as I remember it suggested that this method of payment was now so large as to constitute \$300,000,000 annual payments to patients. The sum struck me as very large since it is something like 30 per cent of all the payments made to physicians about 1928.

I think the context was misleading since I find that in the statement made by the Bureau of Medical Economics in their pamphlet to which you refer it is quite obvious that their pamphlet represents a great variety of payments—many—and possibly most—of which are not made as cash indemnity for medical service as one ordinarily thinks of it. Clearly they have included here all the medical benefits paid under life insurance. It looks to me as if they had included payments made under workmen's compensation acts and, from the loose way in which the sentence is worded, I think it probably includes a great many things which do not directly bear upon the problem which you were in fact discussing. I come to this conclusion partly because of a compilation made by Professor Millis of the University of Chicago which seemed to suggest that group and individual health insurance issued by the regular insurance companies was not decreasing was diminishing and did not cut a very large figure.

It seems to me important to try to keep separate the payments which have long been made by the insurance companies for accidents and which really do not help out very much in providing medical care which can by any stretch of the imagination be called "good." As a matter of fact, most of the accident policies are carried by people who are in relatively good circumstances, or by corporations protecting themselves under the workmen's compensation acts.

HUGH CAROT M.D.

Soldiers Field
Boston

The sentence in *Organized Payments for Medical Services* (Chicago American Medical Association 1939) to which the editorial and Dr. Carot's letter refer reads as follows:

An estimate of the amount of cash benefits paid to members of medical service plans including all types of plans—group and individual accident and health insurance disability benefits under life insurance, mutual benefit, fraternal and trade union plans, and other cash indemnity medical service plans—would be approximately \$300,000,000 annually

En.

CARROT ADDICTION

To the Editor There are many kinds of addictions but this is the first time I have found one for carrots.

REPORT OF CASE

H. W., a forty-two-year-old man, came for examination in August, 1932 because of a canary yellow pigmentation

of the skin of the entire body there was no unginger of the sclerae. Bile pigments were absent in the blood and urine, and serum carotin was present. According to the history he had been told by a physician four years before that carrots would be beneficial. Since that time he had eaten four bunches daily as secured in the market. On being informed as to the cause of his trouble, he left stating he could not stop eating carrots. Attempts to locate him to learn of the eventual outcome have been unsuccessful.

HENRY G. HADLEY M.D.

1252 Sixth Street, S.W.
Washington D.C.

NOTICES

ANNOUNCEMENT

CHARLES DIERF M.D., announces the opening of an office at 1159 Hancock Street, Quincy

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday November 8 from 2 to 4 p.m. Drs. Elliott C. Cutler and Soma Weiss will speak on "Malnutrition." A clinicopathological conference, conducted by Dr. Elliott C. Cutler will take place from 4 to 5 p.m.

On Thursday November 9 from 8:30 to 9:30 a.m. there will be at the Children's Hospital a combined clinic, conducted by Dr. William E. Ladd, of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend

ELLIOTT C. CUTLER, M.D., Secretary

BOSTON CITY HOSPITAL

The monthly clinicopathological conference will be held at the Boston City Hospital on Wednesday November 8 at 12 o'clock noon, in the Pathological Amphitheater

JOSEPH E. HALLISEY M.D., Secretary
Medical Staff

BOSTON CITY HOSPITAL

A meeting to commemorate the completion of twenty five years of the Social Service Department of the Boston City Hospital will be held in the Cheever Amphitheater on Wednesday November 8, at 8:30 p.m.

Hon. Mayor Maurice J. Tobin, Mr. Carl Dreyfus and Dr. Conby Robinson of Baltimore, will be the speakers.

Tickets for admission may be obtained from the Social Service Department, Boston City Hospital. Doctors, social service workers and others interested are cordially invited to attend.

TUMOR CLINIC, BOSTON DISPENSARY

Each Tuesday and Friday morning, 10:00 to 12:30 there is a meeting of the Tumor Clinic of the Boston Dispensary a unit of the New England Medical Center. Neoplasms of various sorts are seen and discussed and when there is an indication are treated with radium of high-voltage x-ray. Physicians are invited to visit this clinic. They may bring patients for aid in diagnosis or may refer patients to the clinic following which a report will be returned to the referring physician. A limited number of beds are available for diagnostic study and for treatment.

school of recognized (Class A) standing with the degree of M.D. subsequent to May, 1919, for medical officer, subsequent to May, 1932, for associate medical officer. Applicants for the position of senior medical officer are not required to have been graduated within any specified time limit.

Further information and the necessary forms may be obtained from the Secretary, Board of United States Civil Service Examiners, at any first-class post office, from the United States Civil Service Commission, Washington, D. C., or from the United States Civil Service district office.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, NOVEMBER 6

MONDAY NOVEMBER 6

- *12 15 p.m.—1 15 p.m. Clinicopathological conference Dr S Burt Wolbach Peter Bent Brigham Hospital amphitheater
- *4 p.m. Physicians and medical students are cordially invited to attend a clinic presented by the medical surgical and orthopedic services of the Infants and Children's hospitals in the amphitheater of the Children's Hospital

TUESDAY NOVEMBER 7

- *9-10 a.m. Is There an American Method of Treating Fractures? Dr Charles L. Scudder Joseph H. Pratt Diagnostic Hospital
- *10 a.m.—12 30 p.m. Boston Dispensary tumor clinic
- *12 15 p.m.—1 15 p.m. X-ray conference. Dr Merrill C. Sosman Peter Bent Brigham Hospital amphitheater
- *4 p.m. Phi Delta Epsilon Fraternity Lectureship Tufts College Medical School
- *5 p.m. Peter Bent Brigham Hospital Research conference of the Medical Staff Amphitheater
- 8 15 p.m. Greater Boston Medical Society Beth Israel Hospital auditorium

WEDNESDAY NOVEMBER 8

- New England Society of Physical Medicine Hotel Kenmore Boston
- *9-10 a.m. Hospital case presentation Dr S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital
- *12 m. Clinicopathological conference Children's Hospital Amphitheater
- 12 m. Boston Gastroenterological Society Boston City Hospital Dowling Amphitheater
- 12 m. Boston City Hospital Monthly clinicopathological conference Pathological Amphitheater
- *2 p.m.—4 p.m. Joint medical and surgical clinic Peter Bent Brigham Hospital
- 8 30 p.m. Boston City Hospital Meeting to commemorate the completion of twenty five years of the Social Service Department Cheever Amphitheater

THURSDAY NOVEMBER 9

- New England Society of Physical Medicine Hotel Kenmore Boston
- 8 30 a.m. Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital at the Children's Hospital
- *9-10 a.m. Pediatric case discussion Dr Francis C. McDonald Joseph H. Pratt Diagnostic Hospital

FRIDAY NOVEMBER 10

- New England Society of Physical Medicine Massachusetts Institute of Technology Cambridge
- *9-10 a.m. Medical Eponymology Dr Robert W. Buck Joseph H. Pratt Diagnostic Hospital
- 10 a.m.—1 30 p.m. Boston Dispensary tumor clinic

SATURDAY NOVEMBER 11

- 10 a.m.—12 m. Medical staff rounds of the Peter Bent Brigham Hospital Conducted by Dr Soma Weiss

Open to the medical profession

- NOVEMBER 3—William Harvey Society Page 676 issue of October 26
- NOVEMBER 3-4—American Sanatorium Association Page 676 issue of October 26
- NOVEMBER 3-29—Joseph H. Pratt Diagnostic Hospital Medical Conference Program Page 718
- NOVEMBER 6-8—American Academy of Dermatology Page 676 issue of October 26
- NOVEMBER 6-11—New England Medical Center Teaching Clinics on Cancer Page 733 issue of October 19

NOVEMBER 7—Greater Boston Medical Society Page 676 issue of October 26

NOVEMBER 7—Phi Delta Epsilon Fraternity Lectureship Tufts College Medical School Page 718

NOVEMBER 7—Peter Bent Brigham Hospital Research conference of Medical Staff Page 718

NOVEMBER 8—Boston City Hospital Monthly clinicopathological conference Page 717

NOVEMBER 8—Peter Bent Brigham Hospital Joint medical and surgical clinic Page 717

NOVEMBER 8—Boston City Hospital Meeting to commemorate the completion of twenty five years of the Social Service Department Page 718

NOVEMBER 8 9 10—New England Society of Physical Medicine Page 718

NOVEMBER 8—Boston Gastroenterological Society Page 675 issue of October 26

NOVEMBER 9—Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital Page 717

NOVEMBER 9—Pentucket Association of Physicians 8.30 p.m. Bartlett Haverhill

NOVEMBER 13—Massachusetts Tuberculosis League Page 718

DECEMBER 2—American Board of Obstetrics and Gynecology Page 676 issue of June 15

DECEMBER 8—William Harvey Society Page 676 issue of October 26

JANUARY 6 JUNE 8-11 1940—American Board of Obstetrics and Gynecology Page 160 issue of July 27

JANUARY 22-25 1940—American Academy of Orthopaedic Surgeons Hotel Statler Boston

MARCH 2 JUNE 8 and 10—American Board of Ophthalmology Page 676 issue of June 15

MARCH 7-9 1940—The New England Hospital Association Hotel Statler Boston

MAY 14 1940—Pharmacopoeial Convention Page 894 issue of May 14

JUNE 7-9 1940—American Board of Obstetrics and Gynecology 1019 issue of June 15

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

NOVEMBER 15—Heart Disease in Pregnancy Dr C. Sidney I. Beverly Hospital Beverly

DECEMBER 6—Pyelonephritis and Its Relation to Other Infectious Diseases of the Kidney Dr Soma Weiss Salem Hospital Salem

JANUARY 3 1940—Head Injuries Dr John S. Hodgson State Hospital Haverhill

FEBRUARY 14—Cough Sputum Hemoptysis—How shall they be treated? Dr Reeve H. Betts Essex Sanatorium Middleton

MARCH 6—Experimental and Clinical Considerations of Sulfonamide Treatment of Hemolytic Streptococcal Infections Dr Champ Lynn Hospital Lynn

APRIL 3—Addison Gilbert Hospital Gloucester

MAY 8—Annual meeting Salem Country Club Peabody

HAMPSHIRE

NOVEMBER 8

JANUARY 10 1940

MARCH 13

MAY 8

All meetings are held at 11 30 a.m. at the Cooley Dickinson Hospital Northampton

MIDDLESEX EAST

NOVEMBER 15

JANUARY 10 1940

MARCH 20

MAY 15

Meetings are held at 12 15 p.m. at the Unicorn Country Club Stony Brook

MIDDLESEX SOUTH

NOVEMBER 8—Page 718

PLYMOUTH

NOVEMBER 16—Moore Hospital Brockton

JANUARY 18 1940—Brockton Hospital Brockton

MARCH 21—Coddard Hospital Brockton

APRIL 18—State Farm

MAY 16—Lakeville Sanatorium Lakeville

SUFFOLK

NOVEMBER 29—Scientific meeting Treatment of Syphilis Dr H. Hyman Dr Louis Chargin and Dr William Leifer of New York City

JANUARY 31 1940—Scientific meeting Subject to be announced

MARCH 27—Scientific meeting Symposium on Ulcerative Colitis and Diarrhea Under the direction of Dr Chester M. Jones

APRIL 24—Annual meeting in conjunction with the Boston Library Election of officers Program and speakers to be announced

The New England Journal of Medicine

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VOLUME 221

NOVEMBER 9, 1939

NUMBER 19

MASSACHUSETTS MEDICAL SOCIETY

Section of Pediatrics*

NONSPECIFIC TREATMENT OF PNEUMONIA IN INFANTS AND CHILDREN

FRANCIS C McDONALD M.D.†

BOSTON

THE treatment of pneumonia in infants and children has become increasingly efficient than the last few years. Although we have used specific chemicals and serums for the treatment of pneumonia at the Boston Floating Hospital and use them in selected cases, we have continued the use of nonspecific therapy in the treatment of all infants and children ill with pneumonia. This paper will concern itself with a description of these general nonspecific methods and the results exclusively achieved by them.

The seriousness of pneumonia in infancy and childhood, with all but the more recent methods of treatment, was well stated in 1916 by Morse,¹ who said: "Pneumonia is a comparatively mild disease in childhood. It is the exception for a child to die of an uncomplicated pneumonia. In infancy, however, pneumonia is a very serious and often fatal disease. The mortality in hospitals varies between 25 and 33 per cent. The following series of pneumonia patients under two years of age treated by nonspecific means confirm Morse's estimates."

Kohn and Wiener² 1926-1933 534 cases, mortality 37 per cent.

Nemir, Andrews and Vinograd³ 1931-1935 526 cases, mortality 31 per cent.

McNeil, Macgregor and Alexander⁴ 1921-1928 310 cases, mortality 44 per cent.

The efficacy of treatment that is restricted to nonspecific means as carried out in the Boston Floating Hospital from 1932 through the first four months of 1939 may be judged from Table 1.

This section meeting was held and the following three papers read at the annual meeting of the Massachusetts Medical Society, Worcester, Massachusetts, June 6, 1939.

†Assistant professor of pediatrics, Tufts College Medical School; assistant to the physician-in-chief, Boston Floating Hospital.

These patients came chiefly from the economically handicapped average family was composed of six to eight persons, the average income was under fifteen dollars a week, and the average rent for living quarters was under fifteen dollars a month. For the most part the homes were located in crowded low rental districts of Metropolitan Boston.

The methods which we used to increase the resistance of infants and children by nonspecific means were those that conserve the energy of

TABLE 1 *Pneumonia Cases by Years*

YEARS	1 YRS (UNDER 2 YRS.)			CHILDREN (2-12 YRS.)		
	NO. OF CASES	NO. OF DEATHS	PERCENT AGE MORTALITY	NO. OF CASES	NO. OF DEATHS	PERCENT AGE MORTALITY
1932	65	20	30	42	0	0
1933	36	9	25	25	2	8
1934	43	7	16	24	0	0
1935	70	7	10	45	0	0
1936	92	10	11	68	4	6
1937	73	7	10	24	0	0
1938	43	0	0	50	1	2
1939 (4 mo.)	50	2	4	26	0	0

the patient, those that provide ample nutrition and those that seem to raise immunologic resistance to the invading organism.

One of the most important principles of the nonspecific therapy of pneumonia was conservation of the patient's energy. The measures employed included increasing the oxygen of the inspired air, judicious use of sedatives and efficient nursing care.

Tissue anoxia produces a sequence of events similar to functional hyperemia caused by inflammation. Moon⁵ states: "Once the lack of oxygen in a large area of tissue reaches the point where capillaries and venules lose their tonus and become abnormally permeable plasma

escapes into the tissues and blood corpuscles are concentrated into minute vessels. This further impedes the circulation and decreases the volume flow, lowers the blood volume and increases the anoxia. With increasing anoxia the re-establishment of circulatory efficiency becomes progressively more difficult. This conception of the effect of anoxemia prompts a liberal use of oxygen for pneumonia, particularly during infancy when the pathologic effect of anoxemia may blend with that produced by the infection.

The average amount of oxygen used per patient at the Boston Floating Hospital is shown in Table 2. Commercial oxygen, which is just

TABLE 2 *Oxygen Consumption and Transfusion Data*

YEAR	AVERAGE AMOUNT OF OXYGEN USED PER PATIENT (ALL AGES) cu ft	PERCENTAGE TRANSFUSED (UNDER 2 YR)	PERCENTAGE MORTALITY (UNDER 2 YR)
1932		30	30
1933		53	25
1934	200	32	16
1935	200	71	10
1936	500	71	11
1937	600	76	10
1938	400	70	0
1939	400	93	4

is good for these purposes as the chemically pure product, was purchased for one cent a cubic foot in tanks holding 220 cubic feet. A concentration of 40 to 60 per cent oxygen in a suitable tent may be maintained for twenty-four hours with about 300 cubic feet of oxygen. Gas under such great pressure as exists in the tank requires the use of a good reducing valve, which costs at least twenty-five dollars. A motor-driven unit required for cooling and circulating the air-oxygen mixture costs one hundred dollars and a tent enclosure an additional fifty dollars. G. W. Ettinger of the Boston Floating Hospital staff has built both these for us. In their construction he used a copper coil, a steel container and a second-hand vacuum-cleaner motor, all these materials cost only twelve dollars. For the tents he used a cellophane-like material (Transental cloth), fifty yards (costing nineteen dollars) being sufficient for seventeen tents. The frames were made of strip iron.

In carrying out the therapy, the oxygen of the inspired air was measured and recorded at least every two hours. For this purpose a simple apparatus devised by Emerson and Company, of Cambridge, Massachusetts, was used. A sample of the air-oxygen mixture near the patient's face was drawn into a 10-cc. syringe. This mixture was introduced through a small glass tube into a testing solution made up of saturated ammonium chloride three parts and ammonia water (28 per

cent) one part. Copper shavings (1 scouring cloth is quite suitable) were immersed in the fluid. After two or three minutes the unabsorbed gas in the cylinder was redrawn into the syringe, all the oxygen having combined with the copper. The accuracy of the testing solution was checked with room air. Regular checking of the inspired air-oxygen mixture is essential, and if necessary the ratio of oxygen to air should be stepped up in order to maintain the desired level, a few hours of anoxemia during a critical period may prove fatal. The danger of explosions, resulting from the use of oxygen under pressure, should always be kept in mind.

A relative humidity of 40 to 50 per cent makes breathing easier and permits better drainage of secretions from the respiratory tract. The humidity within the tent should be measured once or twice a day by means of a wet-and-dry-bulb thermometer. The humidity is generally found to be within the desired range if the temperature in the tent is kept between 75 and 80°F. Under these conditions all clothing may be removed from the chest and abdomen, which permits greater freedom of movement. This also gives the physician and nurse a better opportunity of observing the respiratory movements.

Older children were allowed to assume the position of choice; infants were placed in various positions, until the most comfortable one was found. Many children and older infants assumed the knee-chest position. Small infants generally seemed more comfortable lying prone with the head lower than the chest, but some of them breathed more easily in a supine position with the shoulders elevated and the head and neck in partial extension. Removal of tenacious secretion from the upper respiratory tract by a suction machine or an aspirating bulb usually induced peaceful sleep.

Sedatives judiciously used aid in conserving the energy of a pneumonic infant or child. Morphine sulfate is our choice. The variation of effect produced from patient to patient and from dose to dose is less marked with morphine sulfate administered subcutaneously than with other drugs given by the same or other routes. A rapid, shallow type of breathing with a quick inspiratory effort immediately following expiration generally becomes deeper and more relaxed with this sedative. This makes oxygen therapy more effective. Moreover, morphine used in connection with oxygen therapy usually changes a struggling, frightened child who is not taking enough nourishment to one who is well poised, partially relaxed and eager for food.

Morphine sulfate was given according to the

body weight, 1/6 gr for a 75-pound child, 1/12 for a 30-pound child, 1/24 for a 15-pound infant and so on. Except under unusual circumstances no more than two consecutive doses at four-hour intervals were ordered without seeing the patient. Reaction to the morphine was carefully observed, especially that due to the first dose. Idiosyncrasies usually manifested by marked excitability occurred in about 2 per cent of the patients.

All sedatives are contraindicated if there is difficult breathing caused by tenacious secretion, peripharyngeal or retropharyngeal swellings, severe tracheobronchitis or rapid accumulation of air or fluid in the pleural space, and they of course, should not be given to moribund patients or to those who are in the excited stage preceding collapse from anoxemia. Morphine generally masks the pain due to *otitis media* with the exception of those cases in which swallowing is painful because of referred pain via the glossopharyngeal nerve, consequently the complication of acute *otitis media* should always be looked for and treated appropriately. The responsibility for the use of sedatives for an acutely ill infant or child should rest entirely on the physician.

The standard of nursing care depends chiefly on the physician's anticipating the difficulties that may be encountered and also on the example he sets. For instance, if he removes an anoxic patient from the tent for long periods without evident concern the nurse is apt to do likewise. In some hospitals where medical supervision is not rigid and lay or nursing administration has taken over details of medical supervision physicians may have difficulty in establishing a physician-nurse relation that affords the optimum conditions for proper protection of the patient. Rapid changes in nursing personnel are particularly bewildering, but good descriptive nursing notes, well supervised by reliable ward supervisors, help to overcome this difficulty. Above all gentleness, patience and a sense of responsibility are essential qualities.

The nutrition of an infant or child with pneumonia is of great importance in treatment. Consequently the nutritional history and the physical signs pertinent to it were closely studied. Particular attention was given to the family income with the idea of determining its adequacy for all members of that family. The family's habits of purchasing, storing and preparing its food were investigated in order to find out whether the diet contained the proper proteins, minerals and vitamins. The eating habits of mother and child were scrutinized. All these matters were investigated by the staff and by the visiting nurse, who went to the home of almost every patient for

this information, not only for its bearing on the present illness but also because of its value in preventing other illness which might have a nutritional background.

In planning for proper nutriment during the acute illness, the emergency of preserving life and combating the infection outweighs the needs for optimal growth and development. Proteins and fats are not easily digested, consequently readily digestible and assimilable carbohydrates were given. This prevents unnecessary depletion of protein and provides a better source of energy during the acute illness when metabolism is increased.

Fluids should be given in ample amounts. A mixture consisting of one part normal saline, two parts fruit juice and three parts 10 per cent glucose was commonly used. Since this mixture contains food it was usually not given oftener than every four hours, the total amount for twenty-four hours ranging from 500 to 700 cc. Water should be given between feedings to make up a daily fluid intake of 1000 to 1500 cc. The patients were not disturbed during the night for feeding if sleep was sound and effective and the fluid intake reasonably adequate during the day. Whey and broth were often preferred by the older children. Large amounts of glucose mixtures in concentrations above 5 per cent were avoided because they produced abdominal distention and the passage of frothy, green, acid bowel movements. The daily intake of sodium chloride was approximately 0.1 gr per pound of body weight but with this amount of salt in patients with a low serum protein or excessive anoxia edema occasionally resulted. As a source of vitamin A a concentrated fish oil was given at least 16,000 international units, this also provided an adequate amount of vitamin D. Fifty international units of vitamin B₁ for each 100 calories in the diet was given which was double the estimated daily requirement. If there was any reason to suspect deficiencies in the other known components of the vitamin B complex these were also given. (During convalescence all patients were provided with natural foodstuffs rich in the whole vitamin B complex.) One hundred milligrams of ascorbic acid was given daily.

The use of properly matched adult blood is an accepted means of counteracting a secondary anemia, raising the level of the serum protein and supplying factors that increase immunologic resistance. Table 2 also shows that we have steadily increased the number of transfusions given in infants suffering from pneumonia. This action was taken because of the poor nutritional background of most of our patients, and because of our belief that resistance to the common bacterial invaders

is enhanced by immune factors present in average adult blood. The transfusions were generally given about twelve hours after admission; reactions were rare. It was considered a violation of the general principle of the conservation of the patient's energy to remove him from the oxygen tent during a transfusion. The seriously ill patients were transfused through the ankle vein while still in their tents. In many cases a clinical response by crisis, similar to that seen after specific serum therapy, followed transfusion. It was also thought that convalescence was more prompt and recurrences less common, proof of this, however, is lacking, for no control studies have been made. During convalescence, iron was administered orally if there was secondary anemia.

Pneumonia in infants under three months of age often presents a special problem in diagnosis. The onset may be without fever but with such gastrointestinal symptoms as vomiting and diarrhea. In these patients physical signs of pulmonary infection are delayed, and the dehydration that follows loss of fluids and electrolytes commonly equals about one fifth of the normal body weight. In our experience clinical estimation of the degree of dehydration and the associated chemical disturbances is difficult and the potential danger of the infection may not be suspected. Consequently there is a tendency to delay energetic therapy. For these reasons the management of this group was somewhat different from that of the typical pneumonia patient. Weighings were made every four hours to determine the degree of dehydration and the need for fluids. Continuous use of oxygen therapy, parenteral administration of nutrition and blood transfusions were all started promptly.

SUMMARY

In this series of cases the mortality from pneumonia was greatly reduced without the aid of specific chemicals or serums. This does not imply that these specific methods are not of value, for we now use them in almost every case.

The fact is emphasized that the nonspecific form of treatment is of the utmost importance and should be given consideration in the treatment of pneumonia in infants and children.

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THE SIGNIFICANCE OF TYPE 14 PNEUMOCOCCUS INFECTION AND THE THERAPEUTIC VALUE OF SPECIFIC RABBIT SERUM FOR THIS TYPE OF PNEUMONIA IN INFANTS AND CHILDREN*

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BOSTON

SINCE the classification of the heterogeneous Group IV pneumococci into serologically distinct species (Types 4-32),¹ Type 14 has become recognized²⁻⁴ as the pneumococcus most frequently responsible for pneumonia during infancy and the early years of childhood. The purpose of this paper is to direct attention to the frequency of age incidence and pathogenicity of the Type 14 pneumococcus as it occurs in patients under twelve years of age, and to show the results obtained at the Infants and Children's hospitals, Boston, in the treatment of this type of pneumonia with concentrated specific rabbit serum.

DETAILS AND METHOD OF STUDY

During the last two and a half years, pneumococcus typing has been included as part of the bacteriological investigation of all patients with pneumonia admitted to the Infants and Children's hospitals. Cases with other forms of respiratory or focal infection have been similarly studied. Only infants and children in the first twelve years of life have been included in this report.

Sputum for cultures from patients diagnosed or suspected of having pneumonia was obtained as soon as possible after entry. With a tongue depressor the patient was induced to cough or gag and the mucoid secretions raised were caught on a sterile cotton swab. This swab was placed at once in a centrifuge tube containing suitable culture medium and the tubes were incubated at 37 C. Sterile ascitic fluid obtained by abdominal paracentesis from young children with nephrosis was found to be an efficacious culture medium for this purpose and was used almost exclusively. An optimum growth of pneumococci for typing was usually obtained within two to six hours. The Neufeld⁵ method of rapid typing was employed routinely for identification of any pneumococci present in the cultures. Material from other sources, such as pus from the ears, was similarly cultured and occasionally typings were performed directly on the throat swab mucus or purulent body fluids. Cultures of the blood from nearly all patients with pneumonia were taken at the time of entry or immediately prior to serum therapy. Additional cultures were made if the patient failed to improve or when earlier cultures showed growth of organisms. In order to detect mixed infection with more than one type of pneumococcus, each typing was carried out through all the Neufeld pools and for each constituent type in every pool which gave a positive *Quellung*. Blood type plates were streaked in order to identify and establish the significance of any other associated organisms. In each

case an attempt was made to evaluate the relative importance of all organisms cultured from various sources.

Examination of the chest by x-ray photography or fluoroscopy was obtained as soon as possible after entry so as to confirm, establish or exclude the presence of pneumonia, and repeated examinations were made as deemed advisable. In practically all the patients with Type 14 pneumonia the diagnosis was confirmed by roentgenological evidence.

No attempt was made to classify separately bronchopneumonia and lobar pneumonia. From comparison with the cases of pneumonia due to pneumococcus Type I the

RELATIVE FREQUENCY OF PNEUMOCOCCUS TYPES OBTAINED FROM 608 PATIENTS
JANUARY 1937 JANUARY 1939

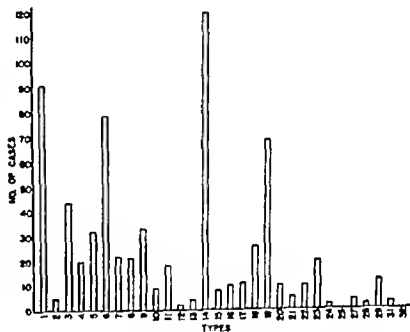


FIGURE 1

pulmonary distribution seemed to be related somewhat to age, the younger patients tending to have atypical pneumonias and the older ones a more truly lobar involvement. The type of organism responsible and the age of the patient appeared to be of more fundamental as well as of more practical importance as a basis for classification and prognosis than the necessarily arbitrary distinction based on the distribution of the pulmonary lesions.

Twelve of the 14 patients with pneumococcus Type 14 infection who died came to autopsy and through the courtesy of Dr. Sidney Farber of the Pathology Department the postmortem findings have been incorporated with the data obtained during life.

PNEUMOCOCCUS TYPE 14 INFECTION

From January 1937, to January 1939, pneumococci were isolated from 608 patients with various forms of infection (Fig. 1), including approximately 400 with pneumonia. Pneumococcus Type 14, obtained from 120 or 20 per cent of all

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†This paper was presented at a meeting of the American Pediatric Society, April 27, 1939, in Skipton, Pennsylvania, and has been published in abstract (Am. J. Dis. Child. 59:656-658, 1939).

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the cases and from 104 or 25 per cent of those with pneumonia, was the most frequent single type encountered and the dominant pneumococcal agent of pneumonia. The conditions with which the Type 14 pneumococcus was found to be associated are presented in Table 1, and the sources

the hospital. Four other infants from whom this organism was obtained in throat cultures had bronchitis and peribronchitis with associated upper respiratory infections, but without sufficient clinical or roentgenological evidence to establish the presence of a definite pneumonic

TABLE 1 Conditions Associated with *Pneumococcus* Type 14

DISEASES	TOTAL NO OF CASES	NO OF DEATHS	AUTOPSIES	INFANTS (UNDER 2 YR.)		CHILDREN (2-12 YR.)	
				NO OF CASES	NO OF DEATHS	NO OF CASES	NO OF DEATHS
Pneumonia	104	10	9	63	8	41	2
Meningitis	4	4	3	4	4	0	0
Miliary tuberculosis	1	0*	0	1	0	0	0
Bronchitis bordering on interstitial bronchopneumonia	4	0	0	4	0	0	0
Otitis media with associated upper respiratory infection	4	0	0	3	0	1	0
Siblings of patients with Type 14 pneumonia all with upper respiratory infection	3	0	0	0	0	3	0
Totals	120	14	12	75	12	45	2

*Patient died two weeks after discharge from the hospital

from which this organism was obtained are noted in Table 2.

Pneumococcus Type 14 occurred predominantly in patients with pneumonia and was invariably associated with some form of respiratory infection. Of the 16 patients in the present series

TABLE 2 Sources of *Pneumococcus* Type 14

WHEN OBTAINED	SOURCE	IN 104 CASES OF PNEUMONIA		IN 16 CASES WITHOUT DEFINITE PNEUMONIA	
		NO OF CASES	NO OF POSITIVE SPECIMENS	NO OF CASES	NO OF POSITIVE SPECIMENS
During life	Throat (sputum)	97	103	10	10
	Blood	8 (of 86 cases)	14	4	4
	Chest fluid	4	11	0	0
	Ears	19	28	5	7
	Mastoid	1	1	0	0
	Spinal fluid	0	0	4	4
	Septic joint	1	1	0	0
Postmortem (9 cases pneumonia, 3 cases meningitis)	Heart's blood	5 (of 7 cases)	5	3	3
	Lung	3	3	1	1
	Pleura	4	4	0	0
	Pericardium	3	3	0	0
	Mediastinum	1	1	0	0
	Ears	5	8	1	2
	Brain	2	2	0	0
Single source during life	Meninges	1	1	2	2
	Spinal fluid	0	0	2	2
	Multiple sources during life	20		1	
	Only at autopsy	3			
During life and at autopsy		5		3	

considered not to have definite pneumonia, 4 were infants with meningitis secondary to infection of the upper respiratory passages. All the patients with meningitis also had bacteremia, none received specific serum therapy, and all died. *Pneumococcus* Type 14 was isolated from the throat of an infant with miliary tuberculosis who died at home two weeks after discharge from

process. One of these patients was ill simultaneously with *Sonné* dysentery. Three infants and a three-year-old child had purulent pneumococcal Type 14 otitis media with associated upper respiratory infection. In addition the Type 14 pneumococcus was obtained in throat cultures from young children with upper-respiratory infection who were siblings of patients in the hospital with Type 14 pneumonia.

As noted in other clinics,^{4, 5} the Type 14 pneumococcus showed an extraordinarily selective distribution and pathogenicity among infants and young children of pre-school age, yielding its dominance among older children to the Type 1 pneumococcus. This is strikingly illustrated by comparing the age incidence of infection with these two types (Fig. 2). Among the patients from whom the Type 14 pneumococcus was isolated the age incidence was similar in the serum-treated and non-serum-treated groups of pneumonia patients as well as in the small group of patients without pneumonia (Fig. 3). Eighty per cent of all the patients and 79 per cent of the pneumonia patients from whom this organism was obtained were in the first three years of life. With one exception fatalities occurred exclusively in this age period.

In adults the Type 14 pneumococcus has been uncommon as the cause of pneumonia, accounting for only 3 per cent of the cases from which pneumococci have been isolated.^{4, 7, 8} The frequency of its occurrence in the nasopharyngeal flora of healthy adults has not been clearly established. Among infants and children the Type 14 pneumococcus apparently occurs infrequently in the absence of pneumonia. Nemir and her asso-

cases⁵ at Bellevue Hospital studied bacteriologically 425 patients without pneumonia and found this organism in only 4.7 per cent of their cases. Long et al.⁶ cultured the nasopharyngeal flora of all patients admitted to the Infants' Hospital, Bos-

ton, caring for infants with pneumococcus Type 14 pneumonia, contracted the disease and succumbed. In 3 additional patients from whom pneumococcus Type 14 was cultured there was evidence that infection with this organism might have been acquired in the hospital. Recent epidemiological studies of the parents and siblings of patients admitted to the hospital for pneumococcus Type 14 infection indicate that family epidemics similar to those reported¹⁰ for other types of pneumococci are not uncommon.

PNEUMOCOCCUS TYPE 14 PNEUMONIA

The factors which appeared to predispose to pneumonia in the 104 patients from whom the Type 14 pneumococcus was obtained are listed in Table 3. Acute upper-respiratory infections including colds, grippe and bronchitis, often with associated otitis media preceded the onset of pneumonia in 66 per cent of the patients. In only 7 per cent was pneumonia secondary to a specific contagious illness or operative procedure. In an additional 13 per cent there existed an associated disease not directly related to the development of pneumonia.

The symptoms which characterized the onset of pneumonia in these cases were somewhat dependent on the age of the patient. In the infants and

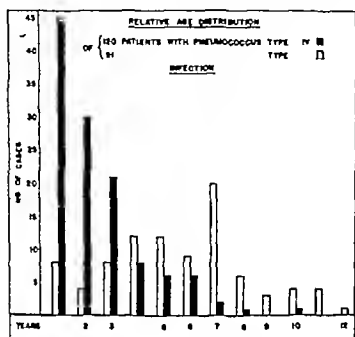


FIGURE 2.

on, during the winter of 1937-1938. They found that Type 14 pneumococci occurred very infrequently in patients with conditions other than pneumonia and never encountered this organism

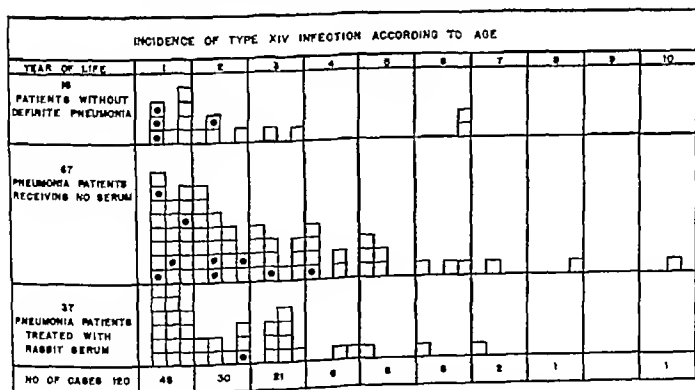


FIGURE 3

Each square represents a case and each dotted square a fatality

in a patient without some form of respiratory infection.

The communicability of infection with the Type 14 pneumococcus has been manifested by the development of acute pneumonia apparently due to this organism in 5 patients hospitalized for other conditions and in a student nurse who while

younger children, among whom preceding respiratory infection had occurred most frequently. Increase of temperature, the development of grunting or rapid respirations, refusal of feedings, irritability and the appearance of a greater degree of prostration were the usual manifestations of incipient pneumonia. Of the patients with preced-

ing upper respiratory infection, evidences of pneumonia developed suddenly in 35 and gradually in 34. Of those without antecedent respiratory infection the onset was sudden in 28 and gradual in 7. Vomiting was associated with the onset or

TABLE 3 *Significant Predisposing Factors in 104 Patients with Pneumonia*

PREDISPOSING FACTORS	NO OF CASES	NO OF RECOVERED CASES	DEATHS	POST MORTEM EXAMINATIONS
Antecedent acute upper respiratory infection	69	61	8	7
Primary conditions to which pneumonia was secondary				
Other infections				
Measles	2	1	1	1
Pertussis and mumps	1	1	0	0
Operative procedures				
Mastoidectomy	1	0	1	1
Appendectomy and peritonitis	1	1	0	0
Bronchoscopy*	1	0	1	1
T and A (with abscess)	1	1	0	0
Pre-existing or associated conditions not directly related to the development of pneumonia				
Bronchial asthma	1	1	0	0
Mild scurvy	1	1	0	0
Celiac syndrome*	1	0	1	1
Congenital heart disease	1	0	1	0
Adrenal insufficiency	1	1	0	0
Chronic osteomyelitis of toe	1	1	0	0
Eczema	1	1	0	0
Cervical adenitis	3	3	0	0
Dysentery (<i>B. paratyphosus</i> B)	1	1	0	0
Pyelonephritis	2	2	0	0

*Type 14 was not confirmed at autopsy as the cause of pneumonia in the patient who died following bronchoscopy and the one with celiac syndrome.

the early stages of pneumonia in 43 of the patients and convulsions in 13. Chills were noted in 9 patients, of whom only 2 were infants. Four children complained early of pleural pain. In infants there occasionally was evidence of abdominal or pleural pain which could not be separately distinguished. Meningismus was noted in 16 patients. Delirium was infrequent, but a majority of the patients appeared prostrated or toxic at the time of admission to the hospital.

Cases of pneumonia due to the Type 14 pneumococcus were clinically indistinguishable from those in which other organisms were etiologic. Although severely ill infants with pneumonia were found to harbor the Type 14 pneumococcus more frequently than any other pneumococcus type, the etiologic diagnosis could not be presumed without bacteriological evidence.

The Type 14 pneumococcus when found in infants and children with pneumonia usually appeared to be causative. Andrews¹¹ found it to be one of several types of pneumococcus which, in a similar age group, appeared to be causative in all patients with lobar pneumonia from whom they were recovered. In 62 per cent of the 104 patients with pneumonia in the present series it was the only organism of importance isolated

Among the 40 patients with associated pathogenic organisms (Table 4), pneumococcus Type 14 was apparently causative in 20 cases and a participating invader in 3 others. In 12 patients the relative etiologic importance of the organisms present could not be established, and in only 5 cases did associated organisms appear to be of greater significance. In evaluating the etiologic importance of the several organisms isolated from an individual patient, the relative significance of their respective sources and the clinical response to the administration of specific antiserum were the chief criteria used.

Of the 20 cases with mixed infection in which the Type 14 pneumococcus appeared to be causative, 13 yielded this organism from multiple sources, including culture of the blood, lungs and purulent exudates. In 3 patients

TABLE 4 *Relation of Other Organisms to Pneumococcus Type 14 in 40 Patients with Pneumonia*

OTHER ORGANISMS	NO OF CASES*	PNEUMOCOCCUS TYPE 14 PREDOMINANT	OTHER ORGANISM PREDOMINANT	PNEUMOCOCCUS TYPE 14 AND OTHER ORGANISMS CAUSATIVE	DOUBTFUL FULLY CAUSATIVE
Pneumococcus					
Type 1	1	0	0	1	0
Type 4	1	0	0	1	0
Type 5	1	0	1	0	0
Type 6	5	3	0	0	2
Type 7	1	0	0	0	1
Type 15	1	0	0	1	0
Type 19	3	1	0	0	2
Type 20	1	1	0	0	0
Types 18-19	1	0	0	0	1
Hemolytic streptococcus	9	5	2	0	2
Hemophilus influenzae	8	6	1	0	1
Staphylococcus aureus	18	12	2	0	4
Bacillus paratyphosus B	1	0	0	0	1
PROBABLY CAUSATIVE ORGANISM					NO OF CASES
Pneumococcus Type 14					20
Other organism					5
Pneumococcus Type 14 and other organisms					3
Doubtful which organism					12
Total					40

*The sums of the cases numbered in the columns are in excess of correct totals for each etiologic category as 16 of the patients with mixed infections had more than one other organism associated with pneumococcus Type 14.

the Type 14 pneumococcus was obtained from a more significant source than that of the associated organism and in the 4 other patients the prompt response to specific antiserum was the basis for considering the Type 14 pneumococcus to be etiologic.

In 3 cases pneumococcus Type 14 and the associated organisms appeared to be about equally pathogenic. In 1 of these, which received serum and is considered later in greater detail, pneumococci Types 1 and 14 were both obtained from cultures of sputum and empyema fluid. In another child who appeared desperately ill, pneumococci Types 4 and 14 were obtained simultaneously from repeated sputum cultures. After forty-eight hours of treatment with sulfapyridine and because no evident improvement had occurred, 33,000 units of Type 14 antiserum were administered intravenously. The patient showed improvement in response to this treatment but remained febrile and incompletely cured for several days. As the patient's serum showed strong agglutinins for the Type 14 pneu-

mococcus but none for the Type 4 pneumococcus following serum therapy the evidence of persisting infection was attributed to the latter organism. In the third of these patients, a child with lung abscess and pneumonia, pneumococci Types 14 and 15 were repeatedly obtained in about equal numbers from the purulent material expectorated.

In 12 patients with pneumonia there was insufficient evidence to establish the etiologic predominance of either pneumococcus Type 14 or the associated pathogens. Both organisms were isolated simultaneously from the sputum in 6 cases and from the ears in 3. In 1 patient pneumococcus Type 14 was obtained from the sputum and *Bacillus paratyphosus* B from blood and stool cultures. Two patients with pneumococcus Type 14 in the sputum yielded *Staphylococcus aureus* in single isolated blood cultures. As preceding and subsequent blood cultures were negative in 1 of these patients and the pneumonia terminated favorably by crisis in both the presence of *Staph. aureus* was of doubtful significance.

In only 5 cases did the associated organisms appear to be of greater significance than pneumococcus Type 14. In a child whose initial sputum culture yielded pneumococcus Type 14 ample treatment with Type 14 antiserum failed to cause improvement and pneumococcus Type 5 was subsequently isolated from the sputum and the ear. Regardless of whether or not both organisms involved the lungs, pneumococcus Type 5 apparently accounted for the therapeutic failure of Type 14 antiserum and was therefore assumed to be the dominant pathogen. In an infant who succumbed to pneumonia following bronchoscopy pneumococcus Type 14 was isolated from the throat during life and from the ears at autopsy. *Staph. aureus* obtained from the lungs was regarded as of greater importance, although it may have been present as a secondary or terminal invader. In 2 patients hemolytic streptococci appeared to be of greater significance. In 1 of these who survived, pneumococcus Type 14 was isolated from an ear and a hemolytic streptococcus from the blood stream. In the other case pneumococcus Type 14 was cultured from the throat on the day before death but at postmortem a hemolytic streptococcus was found in the heart's blood and *Staph. aureus* in the lung. In another patient, pneumococcus Type 14 was isolated twice from the throat and once from an ear in association with *Hemophilus influenzae* which was grown on two occasions from the blood stream. While this probably represented actual mixed infection the influenza bacillus was assumed to be predominant.

The severity and long duration of illness in infants and young children with Type 14 pneumonia together with the high fatality rate in infants, which during the first year of these observations approximated 20 per cent, seemed ample indication for more energetic and specific therapy. Detailed consideration of the duration of illness, the incidence of bacteremia and complications, and the fatalities which occurred among these cases will be reserved for comparison until the results of serum therapy have been evaluated.

Patients Treated with Serum

Three patients received experimental unconcentrated antipneumococcus Type 14 rabbit serum early in 1937. Of these, 1 infant responded by crisis, 1 child of two and a half was unimproved

and recovered ultimately by lysis and 1 infant, treated on the fifteenth and sixteenth days of illness in the presence of bacteremia and empyema, continued an uninterrupted decline to a fatal termination one week later. As the details of administration and the antibody content of the serum used in these 3 cases is not known, they will not be included in the subsequent evaluation of serum therapy.

In March, 1938, potent concentrated antipneumococcus Type 14 rabbit serum became available and was subsequently administered to 34 of 46 consecutive patients with pneumonia from whom the Type 14 pneumococcus had been isolated. Among the 34 patients who received concentrated serum, 22 were infants under two years of age and 29 were less than three. Serum therapy was withheld for various reasons from the 12 patients who were not treated during this period, but in no sense do they comprise a control group. Seven of these 12 patients were children over two years of age, 8 entered late in the course of their disease or were recovering at the time serum administration was contemplated. 1 child had mixed infection with pneumococcus Type 15 and an associated lung abscess, following tonsillectomy, 2 patients were treated with sulfapyridine and 1 mildly ill child was asthmatic. None of these 12 patients died, and none developed purulent complications subsequent to hospitalization.

Patients with pneumonia of less than four days duration were deemed most suitable for serum therapy, but because of the recognized hazards of Type 14 pneumonia treatment was not withheld from seriously ill infants and young children

TABLE 5 Duration of Acute Febrile Illness at the Time of the First Injection of Concentrated Antipneumococcus Type 14 Rabbit Serum

DURATION	No. OF CASES	No. OF IMPROVED CASES	No. OF UNIMPROVED CASES
0-1 day	4	3	1
1-2 days	9	5	0
2-3 days	9	9	0
3-4 days	4	4	0
4-5 days	4	3	1
Over 5 days	4	3	1
TOTALS	34	31	3

who entered later in the course of their disease. Only 4 infants received concentrated serum after pneumonia had been present for longer than five days (Table 5).

Before treatment with specific antipneumococcus serum precautions were taken in each case to determine the presence or absence of sensitivity. A careful inquiry was made into the patient's history for manifestations of allergy, and the usual intradermal and ophthalmic tests were car-

ried out with a 1:10 dilution of rabbit serum. During the tests and administration of serum, epinephrine solution was always immediately available. No positive reactions to these tests were encountered.

In every patient receiving serum, treatment was carried out by the intravenous route. Only 1 infant was given a small additional injection intramuscularly. When the antecubital veins were inaccessible, 24-gauge needles were used and the serum was injected into venules of the extremities or scalp. With the patient held by an assisting nurse the technical difficulties of administration never proved insurmountable.

According to the schedule of treatment gradually formulated, an initial small injection of 0.5 to 1.0 cc of serum diluted 1:5 or 1:10 with physiologic saline was followed after intervals of two hours by larger amounts (4.5 to 10.0 cc) of serum similarly diluted, provided no reactions had supervened. With concentrated serum of high potency, it was usually possible to administer an effective therapeutic dose in two injections. When a delayed reaction occurred, subsequent injections were deferred until all untoward manifestations had subsided. Antipyretic drugs were omitted during serum administration in order to avoid confusion of therapeutic effects.

Reactions to serum occurred in 13 of the 34 patients treated. In 6 of these cases the reactions followed administration of one of the first lots of serum used. In 4 patients the reactions occurred during or relatively soon after serum injection. Three of these, characterized by nausea and vomiting, abdominal pain or transient wheezing, were brief and relatively mild. The single severe, immediate reaction, manifested during the course of an injection by collapse and stridor, was promptly relieved by the administration of epinephrine. Nine patients had chills occurring from a half to one and a half hours after a serum injection, and accompanied in 5 of the cases by temperature elevations above 106°F. In only 1 of these patients, however, was the reaction alarming. Factors which appeared to predispose to these delayed reactions were an existing hyperpyrexia at the time of the serum injection, previous spontaneous chills or convulsions, the rapid administration of serum and the use of a lot of serum known to have produced chills previously.

Five patients showed some manifestation of serum sickness. In 3 this was represented merely by a transient rash or elevation of temperature. Two patients developed the classic picture of serum disease with associated fever and discomfort lasting for several days.

Results of Treatment with Concentrated Antipneumococcus Type 14 Rabbit Serum

The usual response to treatment with concentrated antipneumococcus Type 14 rabbit serum was prompt and gratifying, as shown in the representative individual case charts (Fig 4). The

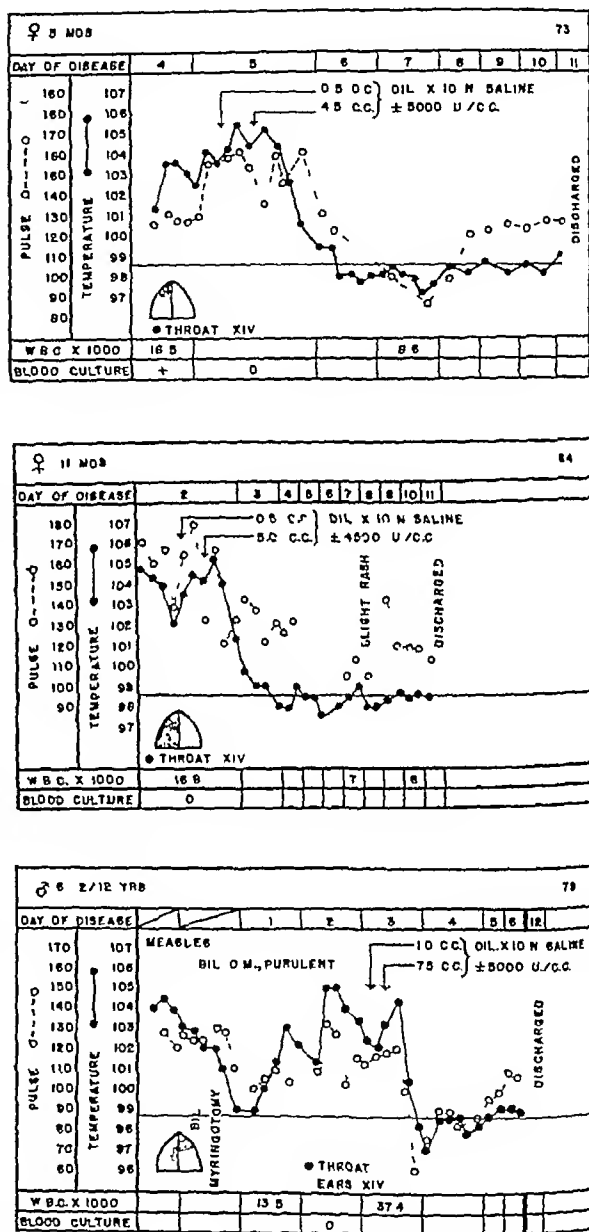


FIGURE 4

improvement was characterized by a decline of temperature, which was frequently dramatic, accompanied or followed shortly by a fall in the pulse and respiratory rates. Subjectively and objectively the patient's general condition gave less tangible but no less striking evidences of benefit. Thirty-one of the 34 patients who received concentrated antipneumococcus Type 14 rabbit serum

appeared to be improved by this form of therapy (Table 6) Twenty four (71 per cent) of the

TABLE 6. Results of Serum Administration*

No. OF CASES	MODE OF RESPONSE	No. INJECTIONS	AVERAGE DOSE	APPROXIMATE AMOUNT OF ANTIBODY
2	Crisis	1	1.5	2,000
24	Crisis (22) lysis (2)	2	7.7	32,000
5	Crisis (2) lysis (3)	3 or more	17.0	66,000
		Average	8.9	36,000

*Excluded are 3 patients who were unimproved by concentrated serum.

patients responded by prompt crisis within six to sixteen hours following the first injection of serum, and to a like number of cases two injections sufficed for administration of an effective therapeutic dose which averaged 7.6 cc. in volume and 32,000 units in antibody content. For the 31 cases which were benefited, 9 cc of serum or 36,000 units of antibody was the average dose employed.

The remaining 3 cases in which concentrated antipneumococcus Type 14 rabbit serum was administered without apparent benefit are summarized below. The failure of serum therapy was attributable in Cases 1 and 2 to the presence of infection with other types of pneumococci, and in Case 3 to the presence of a purulent focus of infection (empyema) at the time treatment was started late in the course of the disease.

CASE 1. A girl of 2 5/12 years was admitted on the day of onset with pneumonia in the right upper lobe. The sputum culture yielded Type 14 pneumococcus. Blood cultures on the 2nd and 4th days of illness were sterile. Concentrated antipneumococcus Type 14 serum was given on the 2nd, 3rd and 4th days of illness (total 30 cc., 135,000 units) without improvement. On the 9th day pus from an ear and retyping of the sputum yielded Type 5 pneumococcus. The patient recovered by lysis after an acute febrile illness of 2 weeks' duration and was discharged on the 27th day.

CASE 2. A boy of 2 9/12 years was admitted on the 3rd day of illness with pneumonia in the left lower lobe. Type 1 pneumococcus was isolated from the sputum. Blood cultures on the 2nd, 6th and 13th days of illness were sterile. Concentrated antipneumococcus Type 1 serum was given on the 3rd and 4th days of illness (total 20 cc., 60,000 units) with only temporary improvement. Retyping of the sputum on the 4th day showed a few Type 1 and many Type 14 pneumococci. One cc. of antipneumococcus Type 14 serum was given on the 4th day but as the patient was found to have developed empyema serum treatment was discontinued. Sulfapyridine was administered from the 4th to the 11th day in doses of 2.4 gm. every 24 hours. Left thoracentesis on the 5th day of illness yielded pus containing only Type 14 pneumococcus, and on the 16th day only Type 1 pneumococcus. Surgical drainage of the pleural cavity was established by a rib resection on the 18th day and the patient was discharged improved on the 42nd day of illness.

CASE 3. A boy of 9 months was admitted on the 9th day of illness with pneumonia in the left upper lobe and roentgenological evidence of fluid along the left axillary border and in the left costophrenic sinus. Type 14 pneumococcus was obtained from the sputum as well as from five cultures of the blood taken from the 9th to the 18th day of illness. On the 21st day *Staph. aureus* was present in a single blood culture, apparently as a contaminant. Cultures of the blood thereafter remained sterile. Massive empyema developed rapidly on the left and was partially drained by thoracentesis on the 13th day. Surgical drain-

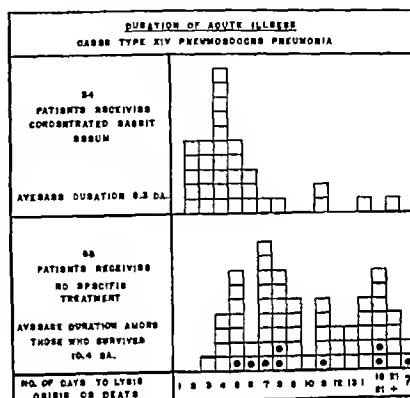


FIGURE 5

Each square represents a case and each dotted square a fatality.

age was established on the 16th day. Concentrated antipneumococcus Type 14 rabbit serum was given from the 9th to the 14th day with only transient clinical improvement. The patient ran a prolonged and stormy course, complicated further by a septic left knee, which was drained surgically after 1 month's illness and yielded Type 14 pneumococcus in pure culture. Sulfapyridine was administered from the 36th to the 53rd day of illness. The patient was finally discharged in good condition after 3 1/2 months of hospitalization.

The results of treatment with concentrated antipneumococcus Type 14 rabbit serum are perhaps most effectively demonstrated by comparing the patients who received this form of therapy with those who did not.

The duration of acute febrile illness for 99 of the 104* patients with pneumonia is represented in Figure 5. Among the non serum treated cases the average duration of acute febrile illness in the surviving patients for whom this could be estimated from the histories given was ten and a half days. In the group of 34 patients who received concentrated rabbit serum this period was

*The 3 patients who received concentrated rabbit serum and the one treated with sulfapyridine alone are not included in Figure 5.

reduced to five and a half days, and for the 31 patients who apparently were benefited to four and a half days. Eighty per cent of the serum-treated patients recovered after an illness of six days or less, whereas only 22 per cent of the non-serum-treated patients recovered in the same period. The long duration of acute illness in the untreated cases was accounted for in most cases

TABLE 7 Complications of Pneumonia in 104 Cases

COMPLICATION	NO OF CASES	NO OF RECOVERED CASES	DEATHS	POST-MORTEM EXAMINATIONS
Otitis media non suppurative	28	26	2	1
Otitis media suppurative	41	33	8	8
Mastoiditis	7	3	4	4
Empyema	5	3	2	2
Pleural effusion	4	1	3	3
Fibrinous pleuritis	3	0	3	3
Pulmonary abscess	5	1	4	4
Mediastinitis	4	0	4	4
Pyopneumothorax	1	0	1	1
Pericarditis	5	0	5	5
Toxic leukopenia	1	0	1	1
Tracheobronchitis	1	0	1	1
Jaundice	2	2	0	0
Focal necrosis of liver	1	0	1	1
Sinusitis with ethmoiditis	1	1	0	0
Meningismus	16	16	0	0
Encephalitis	1	1	0	0
Meningitis	2	0	2	2
Pyarthrosis	1	1	0	0

*Of the 41 cases with purulent otitis media cultures were taken during life or at autopsy on 33 from 24 of these cultures including 7 of the 8 patients who came to autopsy. Type 14 pneumococcus was obtained from one or both ears.

not by complications but by continuation of the pneumonic process, with spread to other areas or failure to terminate by lysis or crisis.

Complications (Table 7), with the exception of

in those receiving concentrated serum, save in the 2 patients previously mentioned (Cases 2 and 3), who had empyema at the time antipneumococcus Type 14 serum was first administered.

Pneumococcus Type 14 was grown from the blood of 8 (9 per cent) of the 86 patients with pneumonia from whom cultures were taken during life (Table 8). The 2 infants who received concentrated serum survived, although 1 of them (Case 3) failed to show any immediate benefit in response to serum administration. Two infants who were not treated with concentrated serum, of whom received unconcentrated serum, died. Of the 4 children over two years of age in whom cultures of the blood were positive, none received concentrated serum and 1 died. One of the patients who survived was treated with sulfapyridine.

Among the 70 patients who were not treated with concentrated rabbit serum there were 16 deaths, including 1 of the 3 patients who were given unconcentrated serum early in 1937. Nine of the 10 patients who died were studied at autopsy, and pneumococcus Type 14 was the predominant pathogen obtained from cultures of the blood, lungs and purulent exudates in 4 but the 2 patients mentioned previously. In the 1 fatal case which did not come to autopsy pneumococcus Type 14 was the only organism of significance recovered during life. All the fatal cases examined postmortem had purulent complications secondary to the acute pneumonic process.

The mortality rate in untreated patients, r

TABLE 8 Analysis of Deaths from Pneumonia

CLASSIFICATION OF CASES	TOTAL NO OF CASES	DEATHS	MORTALITY %	INFANTS (UNDER 2 Yr.)			CHILDREN (2-12 Yr.)		
				NO OF CASES	DEATHS	MORTALITY %	NO OF CASES	DEATHS	MORTALITY %
Cases occurring prior to use of concentrated antipneumococcal rabbit serum	58*	10 ²	17	36 ²	8	22	22 ²	2 ¹	9
No specific treatment	55 ¹	9 ³	16	34 ¹	7 ¹	21	21 ²	2 ¹	10
Unconcentrated rabbit serum	3 ¹	1 ¹		2 ¹	1 ¹		1	0	
Cases occurring after March 21, 1938	46 ²	0	0	27 ²	0	0	19 ¹	0	0
Treated with concentrated rabbit serum	34 ²	0	0	22 ¹	0	0	12	0	0
Treated with sulfapyridine alone	2 ¹	0	0	1	0	0	1 ¹	0	0
No specific treatment	10	0	0	4	0	0	6	0	0

*Superscripts indicate the number of cases from which positive blood cultures for pneumococcus Type 14 were obtained during life.
†Concentrated antipneumococcus Type 14 rabbit serum was given to 1 infant who had received sulfapyridine for 48 hours without improvement.

otitis media, which occurred in 66 per cent of all the cases, were relatively uncommon. In many patients otitis media was present at the time of hospitalization and it was impossible to determine whether the otitis occurred as a complication of pneumonia or as a manifestation of preceding upper respiratory infection. Serious complications, although infrequent, almost invariably proved fatal in non-serum-treated patients and did not occur

duced to its lowest terms by exclusion of cases in whom other organisms appeared to be of great significance (Table 4), and those receiving other forms of specific therapy, was 15 per cent for 3 infants under two years of age and 7 per cent for 27 children over two years of age. Among the 34 patients who received concentrated rabbit serum, 22 of whom were infants under two years of age, there were no fatalities.

COMMENT

The Type 14 pneumococcus appears to have its highest incidence and greatest pathogenicity among infants and young children in whom it is the dominant pneumococcal agent of pneumonia. When found in patients of this age group even when associated with other organisms it is usually of etiologic importance in relation to existing pulmonary infection, and it has not been found to occur commonly in the absence of pulmonary infection. As a cause of pneumonia in patients of pre-school age its importance is comparable to that of the Type 1 pneumococcus in adults.

In infants and young children, pneumonia attributable to the Type 14 pneumococcus is usually a severe and prolonged disease. Even with hospital care and good supportive treatment the fatality rate has been relatively high, particularly in patients under two years of age.

Favorable results with the use of horse serum in the treatment of Type 14 pneumococcus pneumonia in infants and children have been reported.^{1, 2, 13-14} Recent investigations into the cause of unusual and sometimes fatal reactions in occasional patients receiving antipneumococcus Type 14 horse serum led to the observation that the serums of horses immunized against Type 14 pneumococci have agglutinins in high titer for human erythrocytes of all four blood groups.¹⁵ In view of these findings the use of available antipneumococcus Type 14 rabbit serums of equal or greater potency which do not possess this property is preferable. Furthermore, rabbit serum may be given safely to patients sensitized to horse serum by previous immunization, and conversely, administration of rabbit serum will not sensitize to horse serum, which may be indicated subsequently for other purposes.

Indiscriminate utilization of serum therapy for mildly or moderately ill children with pneumonia has been wisely discouraged by Nemir¹⁴ who recommends its use only for severely ill patients early in the course of their disease and for infants in whom the mortality is high. However as all pneumococci do not produce pneumonia of like severity and the early clinical appearance of an individual patient may prove deceptive with respect to his ultimate course, the pneumococcus type responsible is another important factor to be taken into consideration. The finding of Type 14 pneumococcus in an infant or young child with definite pneumonia is in itself an indication for specific therapy.

Recent published and unpublished experiences with sulfapyridine in the treatment of pneumonia have indicated that this new chemotherapeutic agent may have a wide range of usefulness, espe-

cially for infants and children. As most of the present group of patients were treated before sulfapyridine became available, no further comment is within the scope of this report other than to emphasize the importance of accurate bacteriological diagnosis for achieving a proper evaluation of its effectiveness.

The 34 patients here reported to whom concentrated antipneumococcus Type 14 rabbit serum was administered were selected as suitable for this treatment from 46 consecutive patients with pneumonia from whom pneumococcus Type 14 had been isolated. Serum was introduced not to substitute for supportive measures of well-established value but to supplement them in an effort to achieve a more effective course of treatment. Although the number of patients who received the concentrated type specific rabbit serum is small and the non serum treated cases analyzed do not represent a properly constituted control, comparison of these two groups affords a basis for tentative conclusions. From the clinical results obtained, concentrated antipneumococcus Type 14 rabbit serum, administered in relatively small doses appeared to be of definite therapeutic value.

SUMMARY AND CONCLUSIONS

In a series of 120 infants and children, including 104 with pneumonia from whom Type 14 pneumococcus was cultured the salient clinical and bacteriological findings have been presented and discussed.

Concentrated antipneumococcus Type 14 rabbit serum was administered to 34 of the patients with pneumonia, including 22 under two years of age.

All the patients who received this form of therapy survived, and all but 3 with complications or mixed infection showed prompt improvement in response to adequate doses.

The clinical results obtained indicate that for the treatment of pneumococcus Type 14 pneumonia in infants and children, concentrated antipneumococcus Type 14 rabbit serum constitutes a valuable addition to the usual modes of therapy.

The author acknowledges his indebtedness to members of the clinical and bacteriological staffs whose co-operation made this study possible, to Dr Maxwell Finland of the Boston City Hospital for his helpful suggestions, to Mrs. Christina Carne for her assistance in preparing the charts and tables and to Dr W. G. Malcolm executive director of the Lederle Laboratories, Incorporated, Pearl River, New York who generously provided the therapeutic serums.

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THE TREATMENT OF PNEUMOCOCCAL PNEUMONIA IN INFANTS AND CHILDREN WITH SULFAPYRIDINE*

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THE advent of sulfapyridine¹ for the treatment of infections due to the pneumococcus and other organisms came at a time when specific anti-pneumococcus serums, including those recently developed against many of the more important higher types of pneumococci (Types 4 to 32) so frequently associated with the pneumonia of infants and children,² were fully justifying their employment on a large scale. Therefore, when sulfapyridine was first introduced at the Infants' and Children's hospitals in Boston in October, 1938, the new drug was administered to only a few carefully selected patients for whom type-specific serum was not available. Their response was so satisfactory that, during the period from December, 1938, to June, 1939, when this study ended, sulfapyridine displaced serum entirely in the treatment of pneumonia due to pneumococci of all types.

The criteria adopted for the employment of sulfapyridine were definite clinical evidence of pneumonia not already in the convalescent stage and the presence of one or more types of pneumococci in the patient's throat. In all, 154 patients

Physical signs of pneumonia in practically all the patients were confirmed by fluoroscopic examination on the ward by one of the hospital residents, and x-ray films of the lungs were taken routinely within twenty-four hours after admission. Only one of the patients in this series received neither examination. The extent of the consolidation in the lungs of all but 15 was noted by both x-ray and fluoroscopic examinations, repeated according to the condition of the patient.

At first only those patients were treated with sulfapyridine from whose throats a typed pneumococcus had been obtained. Later, sulfapyridine was administered to very ill patients on the presumptive evidence that the demonstrated pneumonia was due to the pneumococcus. Treatment was continued only if this impression was confirmed by Neufeld typing of material from the patient.

BACTERIOLOGICAL STUDIES

Material for pneumococcus typing was obtained by placing a sterile swab deep in the patient's pharynx and inducing a cough. A tube of sterile ascitic fluid was inoculated from this swab and incubated for from four to six hours. During this period the pneumococci usually outgrew the other organisms, and it became possible to recognize them and determine their specific types by the Neufeld method (capsular swelling). Occasionally the material from the throat contained enough pneumococci to permit immediate typing.

In this series a justifiable distinction is drawn between infants and children, for the two groups tend to differ not only immunologically,³⁻⁵ but also in respect to the predominant types of pneumococci found in their throats, as well as in their clinical response to infection by these organisms.

TABLE 1 Patients with Pneumococcal Pneumonia Treated with Sulfapyridine

	INFANTS	CHILDREN
Male	43	48
Female	28	35
Totals	71	83
Average age	10.5 mo	4.6 yr

with pneumococcal pneumonia—71 infants and 83 children—were treated with sulfapyridine during this period (Table 1). The pneumonia was considered primary in 151 patients.

*From the Infants' and Children's hospitals, Boston, and the Department of Pediatrics, Harvard Medical School.

†Associate in pediatrics and instructor in bacteriology, Harvard Medical School; associate visiting physician and staff bacteriologist, Infants' and Children's hospitals.

Among the infants under two years of age, for example, Type 14 was by far the commonest, Types 7, 19, 3 and 6, and 4 and 17 following in that order. Types 1 and 2 were not encountered among the infants but all the other types through Type 29, except Types 13, 24, 25 and 28, were found at least once. In the children over two years of age, Type 1 was predominant. Type 14

TABLE 2 Incidence of Multiple Types of Pneumococci in the Same Patient

NO. OF TYPES	IN	TE	CHILDREN
1	51	48	
2	16	18	
3	4	13	
4	1	3	
5	0	0	
6	1	0	
7	0	1	
Totals	73	83	

was the next most frequent occurring especially among the younger children. Then came Types 19, 6 and 7, and, all with equal frequency 3, 10, 16 and 23. The new "Wilder"⁶ strain occurred in 3 children.

In 30 per cent of the infants and 43 per cent of the children more than one type of pneumococcus was recovered from the throat at the same time (Table 2)*.

Since other pathogenic organisms, such as *Staphylococcus aureus*, *Streptococcus hemolyticus* and *Hemophilus influenzae* may invade the lungs along with pneumococci or independently, a blood agar plate was inoculated from a deep throat swab. Although other pathogenic organisms were frequently encountered in such cultures (Table 3), their role was not always clear. In

TABLE 3. Organisms Accompanying Pneumococci in Throat Cultures

ORGANISMS	IN	INFANTS	CHILDREN
<i>Streptococcus hemolyticus</i>	16	19	
<i>Staphylococcus aureus</i>	9	4	
<i>St. hemolyticus</i> and <i>St. ph. aureus</i>	2	0	
<i>Hemophilus influenzae</i>	0	6	
<i>St. hemolyticus</i> and <i>H. influenzae</i>	0	1	
Total	27	30	

at least two instances, however, they seemed to contribute to the fatal outcome, since they were present in the blood stream before death.

The blood cultures of 13 patients were positive (Table 4). All but 3 patients had a blood culture taken before sulfapyridine therapy was started. In no case did the blood culture remain positive for pneumococci after the administration of sulfapyridine.

*Credit for the success in finding these numerous types of pneumococci is due the painstaking work of Dr. W. F. Franke, Dr. F. H. Allen, Dr. C. O. Grover, and Miss Marjorie Sweet in the Bacteriology Laboratory, Children's Hospital.

OTHER LABORATORY PROCEDURES

Complete blood counts and urinalyses were done on admission and an attempt only partially successful, however, was made to repeat these at least every three days. Recently a daily urinalysis as long as the drug is administered and for three days thereafter has been the rule. In most instances the concentration of sulfapyridine in the blood was determined during the height of fever and during convalescence, a convenient micro-method⁷ being used which required only 0.1 cc of blood from a finger or toe.

TREATMENT

Supportive

On admission to the hospital immediate steps were taken to make the patient as comfortable as possible. General supportive measures suited to the particular patient were adopted. Three infants were placed in an oxygen tent soon after admission. Five received blood transfusions at some time during their stay in the hospital. All

TABLE 4. Posture Blood Cultures

ORGANISMS	AGE	OUTCOME
Pneumococcus		
Type 1	2 4/12	Died in 2 wks
Type 1	3 8 2/12	Recovered
Type 4	1 1 4/12 1 5/12	Recovered
Type 14	6/12 1 1/12 1 3/12	Recovered
<i>Streptococcus hemolyticus</i>	1 5/12 2 10/12	Died
<i>St. pharyngococcus aureus</i>	2/12	Died

infants and children who were in a state of ketosis or dehydrated from vomiting or diarrhea or in sufficient fluid intake were given intravenous glucose and saline solutions. Morphine and the barbiturates were not withheld when the patient was in pain or restless. Enemas were given and rectal tubes were used for abdominal distention.

Sulfapyridine

Sulfapyridine⁸ is a white, almost tasteless, crystalline substance,⁹ relatively insoluble in water. Except in a few instances, the drug was administered by mouth in powdered form, mixed with a palatable semisolid food, such as apple sauce or junket, as a vehicle. The sodium salt of sulfapyridine⁹ is very soluble in water and may be given intravenously in a concentration of from 1 to 5 per cent, but owing to its alkaline reaction (pH 10 to 11) it is not suitable for subcutaneous injection in these concentrations. Three patients in this series received one or more intravenous injections of the sodium salt of sulfapyridine. In most cases, sulfapyridine was readily absorbed by mouth. By rectum the absorption

⁸The sulfapyridine used in this study was supplied through the courtesy of the Calko Chemical Company, Incorporated, Tonal, Brook, New Jersey and the Lederle Laboratories, Incorporated, Pearl River, New York.

was found to be irregular and as a rule insufficient for the best therapeutic results. In agreement with the experience of others,¹⁰ a blood level of 4 to 8 mg* per 100 cc appeared to be desirable. In 3 patients the above routes of administration were combined.

Most of the infants were given an initial dose equal to about 1/3 or 1/2 gr of sulfapyridine per pound of body weight, and thereafter 1 1/2 gr per pound per day, in four to six divided doses. Children were given a similar initial dose and thereafter 1 gr per pound per day in divided doses. As a general rule, the drug was discontinued after the temperature had been normal for two or three days or until some complication rendered further therapy with sulfapyridine inadvisable. Sodium sulfapyridine in normal saline solution was given intravenously in a dose of 1/2 gr per pound in a single case, and in a dose of 1 gr per pound in two others. The sodium salt was not given rectally.

CLINICAL RESULTS

The regularity of the clinical response to sulfapyridine was very impressive. Of the 71 infants treated with sulfapyridine (including 1 treated twice and 2 re-admitted), 57 (80 per cent) became afebrile within forty-eight hours, 19 (27 per cent) in the first twelve hours and 19 (27 per cent) more in the next twelve hours. Of the 9 who improved

TABLE 5 Data on Infants Who Died

TYPE OR TYPES OF PNEUMOCOCCI IN THROAT	AGE mo	COMPLICATIONS
Type 21	2	<i>Staphylococcus aureus</i> septicemia and abscesses of lungs (autopsy)
Types 11, 16 and 27	4	Agenesis of the right lung (autopsy)
Type 12	4	Eczema and abscesses of the scalp
Types 6, 8 and 19	8	Amyotonia congenita and <i>Streptococcus hemolyticus</i> septicemia (autopsy)
Types 4 and 6	12	Died less than 4 hours after admission

more slowly, over a period of two to six days, 2 had purulent otitis media, 1 had amyotonia congenita, and 1 received an insufficient dose. Five infants died, all under circumstances such that the outcome could not have been ascribed solely to the failure of sulfapyridine (Table 5).

Of the 79 children, excluding 4 who were essentially afebrile or apparently convalescent at the outset of therapy, 71 (90 per cent) became afebrile within forty-eight hours after sulfapyridine was first administered, over half of these within twenty-four hours. Of the 3 who did not become afebrile until sixty hours had elapsed, 2 suffered from chronic bronchitis. Of the four

*Unconjugated sulfapyridine

whose fever persisted for longer periods (up to six days), 1 child had a plastic pleural exudate and 3 had empyema. The only fatality among the children was a little girl of two and a half years. She was moribund on admission. An emergency thoracentesis was done because of a massive empyema. She developed bilateral pneumothorax and empyema and died after a lingering illness of two months.

There was no apparent correlation between the length of time the patients had been acutely sick before sulfapyridine was begun and the speed with which they responded to the drug, or between the type of pneumococcus and the character of the response.

Although otitis media was present in an undetermined number of the infants (Table 6), and although several patients had pleurisy and

TABLE 6 Complications

COMPLICATION	INFANTS	CHILDREN
Otitis media or mastoiditis or both	?	10
Thickened pleura	9	8
Plastic pleural exudate	0	2
Sterile pleural fluid	0	3
Empyema	1* (no operation)	4† (operation)

*Type 14 pneumococcus

†Three with Type 1 pneumococcus, one with Types 1 and 7

empyema, there was evidence in every case that the complications were present, at least in their incipency, at the time that sulfapyridine therapy was begun. For example, when empyema developed, the admission examination, by physical signs or x-ray, had disclosed thickening of the pleura on that side of the chest or even pleural fluid. With one exception, an infant with Type 14 infection, those patients with frank empyema eventually required operation, in spite of aspiration of the pus and the continued administration of sulfapyridine.

Provided no frank complication was present, the children, once convalescent, usually went on to prompt and complete recovery with the subsidence of the fever. One girl of four and a half years, who responded rapidly to the usual dose of sulfapyridine, was known to have a plastic pleural exudate at the base of the right lung. She was discharged home for further convalescence, but returned twenty-four hours later with a moderate fever. This subsided in two days without the aid of sulfapyridine and the signs of pleural thickening gradually disappeared.

On the other hand, 6 infants exhibited a persistence of the infection or a re-infection in the same parts of the lungs first involved, the sulfapyridine having been discontinued because of apparently satisfactory convalescence. The signs

severe, and all the patients recovered, with no apparent residual renal damage

DISCUSSION

The experience gained from the treatment of this series of infants and children and from the experience of others¹⁰⁻¹² does not as yet enable one to state categorically the optimum dosage and method of administration or to define exactly the full potentialities and the limitations of the drug. It is quite evident, however, that in sulfapyridine an extraordinarily effective agent for the treat-

spond to sulfapyridine, or a known idiosyncrasy or untoward reaction to the drug may now and then call for serotherapy. Furthermore, the possibility that selected cases would profit by the combined use of serum and sulfapyridine must be borne in mind.¹³

RECOMMENDATIONS

An initial dose of $\frac{1}{2}$ gr of sulfapyridine per pound of body weight, by mouth, followed by small divided doses amounting to 1 gr per pound per day for children and $1\frac{1}{2}$ gr per pound per day for those under two years of age, usually results in therapeutically effective blood levels (4 to 8 mg per 100 cc). The drug should be mixed with some semisolid food. At the outset, inability of the patient to retain the drug by mouth or the severity of the illness may occasionally require the intravenous administration of sodium sulfapyridine in a 5 per cent concentration in sterile distilled water, in a dose of $\frac{1}{2}$ or 1 gr per pound. This should be given slowly, with great care not to allow extravasation of fluid from the vein. Intravenous sodium sulfapyridine may be repeated in six or eight hours, but an immediate attempt should be made to have the patient take the ordinary form of the drug by mouth, and in no case should the intravenous administration be continued without determining the concentration of the drug in the blood at frequent intervals.

Failure of the patient to respond favorably within forty-eight hours is an urgent indication not only for a determination of the blood level of the drug as a guide to possible alterations in the dosage, but also for a review of the case as to diagnosis, and especially for a careful search for complications, such as empyema. In uncomplicated cases it is usually advisable to discontinue the drug after the temperature has been approximately normal for one or two days. Under no circumstances should the continuance of the drug in the presence of known complications be allowed to mask the indications for surgical drainage.

Because of possible toxic reactions, a complete blood count at least every three days during the administration of the drug and a daily urinalysis as long as the drug is administered and for three or four days thereafter are strongly advised.

When sulfapyridine is continued for more than two or three days a determination of the blood level will serve as a guide to the daily dosage. Intelligent understanding of the case calls for a blood culture and an examination of material from the patient's throat for pneumococci and for other pathogenic organisms, since the latter may

TABLE 8 Data on Cases with Hematuria

AGE	DAY AFTER FIRST DOSE	BLOOD LEVEL	CLEARED
yr		mg per 100 cc	days
5/12	3	9.2 (3rd day)	<7
2 3/12	5	1	2
5 9/12	6	5.4 (3rd day)	2
2 6/12	3*	11.8 (1st day)	4

*Received large dose first day none thereafter

ment of pneumonia due to pneumococci has been developed. Sulfapyridine has certain advantages over type-specific serums—

1 It is easily administered by mouth (as a rule it does not require venipuncture).

2 With rare exceptions,¹³ it is apparently effective against all strains of pneumococci. This property obviates the need for having available numerous type-specific antipneumococcus serums. When multiple types of pneumococci are present in the throat of the same patient at the same time, one need not attempt to select the most likely type for serotherapy.

3 Its period of greatest effectiveness is not limited to the early stages of pneumonia.

4 It may be given to allergic and serum-sensitive patients. The condition of desperately sick patients is not made more precarious by thermal reactions so common after serum therapy. Except for rare cases, it may be given repeatedly at various intervals.

5 It is also effective against hemolytic streptococci.¹⁴

6 It is relatively inexpensive.

Granting these general advantages of sulfapyridine over serum, the risk of toxic reactions, such as hematuria,¹⁵ granulocytopenia¹⁶ and acute hemolytic anemia,¹⁷ indicates that the use of the drug should be reserved for those infants and children with definite pneumonia due to pneumococci (or hemolytic streptococci) where the severity of the illness justifies the hazards of chemotherapy, slight though these appear to be.

Surgical complications, where vomiting would be detrimental, the failure of the patient to re-

impose their own characteristic features on the course of the disease.

Success with specific measures for the treatment of pneumonia in infants and children has lessened the burden of nursing care and general supportive measures, but the latter are still of fundamental importance. The most effective combination of all the measures suited to the needs of the individual patient still calls for the practice of the art of medicine.

SUMMARY

An analysis of 154 sulfapyridine treated cases of pneumococcal pneumonia in infants and children is presented, with certain recommendations

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DISCUSSION OF PAPERS BY DR. McDONALD CURNEN AND DAVIES

Dr. Maxwell Finland Boston All the problems bear on treatment of pneumonia are much the same in children and in adults, except that they are dealt with in a somewhat special manner. The major problem was well summarized in Dr. Davies's last words, which very aptly covered the whole subject. It is important that in the treatment of pneumonia in children the emphasis be not entirely focused on drug therapy thus eclipsing completely all notion of the care of the patient, and ignoring the fact that there are beneficial methods of treatment which have to be borne in mind at some time or other regardless of how valuable or important any given effective agent is. It is essential to bear in mind that the patient must be treated, and that, since under certain circumstances a particular remedy may not be effective, it is well to be acquainted with other tried

remedies and to be in a position to use them effectively when the time comes.

Dr. McDonald's presentation of the results from the Floating Hospital which showed a striking drop in the death rate with the introduction of transfusion and oxygen therapy plus, of course the improvement in the general treatment of the children is highly significant. To attain a mortality of only 2 per cent in 73 patients under two years of age is quite an achievement, considering all the high death rates in that age group which the speaker has cited from the literature, and which are becoming more and more evident as physicians type their cases and evaluate the death rate on the basis of etiologic agents. We recognize that Type 14 pneumococcus is an important one in children under two, and this particular group has a considerable mortality.

The underlying factors concerning the effective agents in transfusion are very difficult to perceive. No doubt the nutritional value and the oxygen-carrying property of the blood, and perhaps other factors, are important. One interesting feature in which I am particularly interested has been the fact that the Type 14 pneumococcus as you have seen from Dr. Curnen's chart, is not a very prominent type in older children and in adults rarely occurs as the cause of pneumonia. Along with this we find that while infants may have some slight basic immunity to pneumococcus Type 14 adults almost universally have a high grade of immunity. It is very difficult to find 0.5 cc. of blood from an adult which when mixed with virulent Type 14 pneumococci is unable to destroy hundreds of thousands of bacteria in a very short time. When such blood is introduced into the infant it may have some bearing on the outcome, and some of the dramatic crises following transfusions may very well be attributed to that particular property of adult blood.

The demonstration that Dr. Curnen gave of the efficacy of antipneumococcus serum, entirely apart from whether it is the preferred treatment, is certainly impressive and warrants consideration. These results were obtained with rabbit sera. These sera, we must bear in mind have only recently been perfected so that reactions are becoming very uncommon, particularly the severe, allergic, and perhaps fatal type. Even thermal reactions are becoming much less frequent. The sera are now highly potent and highly concentrated. In practically all types they are considerably more effective than before, and dramatic responses are more frequent.

In serum-treated patients there are a minimum of reactions, aside from serum sickness. The latter bothers us very little because it occurs when the patient is well. Usually as Dr. Curnen has pointed out, serum sickness is very easy to treat and we do not worry about it. The dangerous reactions from serum occur while one is treating the patient and is prepared to meet them. This is a factor to be borne in mind, particularly if one is treating a patient in the home. Complications of drug therapy such as hematuria anemia and granulocytopenia may be insidious in their onset, and are likely to appear in patients who are not yet well. The physician may be unable then to differentiate symptoms of pneumonia and those due to the drug. These complications may appear in the intervals between blood counts or urine analyses, and drug therapy may be continued in the meantime to the detriment of the patients. We have seen, and others have described, patients who have developed nitrogen retention and generalized edema and have died with concretions of acetylsulfapyridine crystals in their kidneys.

The fact that untoward effects occur should not deter us from using these valuable life-saving measures but

the toxic effects of the drugs must be borne in mind even in young children, and in spite of the fact that, in general, infants and children tolerate the drug considerably better than do adults.

The fact that some infants and some older children still die from pneumonia does not mean that these particular drugs are not effective. With all important life-saving measures such as specific serums and sulfapyridine there will always be a certain number of deaths. These will occur under unusual conditions, that is, in patients who are neglected and come to treatment late, or in those who have already developed complications of the disease which are not adequately affected by either specific serum therapy or drug therapy. Therefore early diagnosis and the advisability for parents to call physicians as soon as possible are just as important or perhaps more important now than ever before, because we have much to offer. The main thing we have to bear in mind is that we still have to treat our patients and still have to study them. Diagnostic problems, particularly in the course of treatment, have increased rather than decreased as compared with what they were before we had specific serum, and particularly before we had the new chemicals.

A PHYSICIAN I should like to ask Dr. Davies whether he always uses sodium bicarbonate.

DR. DAVIES We have no rule about it. In some cases we give sodium bicarbonate, in others we do not.

DR. JAMES M. BATY, Boston I should like to ask Dr. Davies if at the Children's Hospital sulfapyridine is continued five or six days. Dr. Charles H. Smith, of New York City, reported at a recent meeting that they had arrived at the point of continuing its use only two or at the most three days, and if the temperature was normal or practically normal at that point they omitted the drug and did nothing else. If the temperature was still elevated and the patient was apparently not responding, they omitted the drug and gave specific serum if it was available.

DR. DAVIES It is probably best to continue the drug for two or three days or at least until the temperature has not only reached normal but has remained normal for about twenty-four hours.

DR. BATY Dr. Finland, have you studied the development of antibodies following the giving of sulfapyridine?

DR. FINLAND Yes, we have studied this aspect exten-

sively. In adults, so far as we have been able to ascertain, the development of immunity is the same in patients who have been treated with sulfapyridine as in those who have received no specific therapy. Many develop or have antibodies early, but in some cases the first demonstrable antibodies appear as late as the fourteenth day of illness. Occasionally the patient's temperature has already been normal for a week before specific antibodies are first demonstrated. In some patients relapses of fever have occurred. We have not yet correlated our findings, but relapses of fever, although they do occur, are not so frequent as one might expect from the delay in the development of immunity. It may be that antibodies which are not demonstrated by protection tests are adequate, or else some other mechanism of recovery is involved.

A PHYSICIAN Dr. Davies, have you cured any cases of pneumococcal peritonitis?

DR. DAVIES In the past year we have had, I think two cases which recovered. I think Dr. Curnen can tell you more about them.

DR. CURNEN The one patient I remember who had pneumococcal peritonitis and received sulfapyridine did not provide a satisfactory test of the drug's effectiveness. Pneumococcus Type 6 peritonitis and bacteremia developed suddenly as a complication of nephrosis. The child's treatment included, successively, incision and drainage of the peritoneal cavity, a transfusion with blood subsequently found to possess type-specific antibodies, administration of sulfapyridine and intravenous injection of concentrated type-specific rabbit serum. Prior to the first dose of sulfapyridine the patient appeared to be clinically improved; the temperature had fallen and cultures of the blood had become sterile. The prompt recovery was gratifying, but proved inconclusive with respect to the individual merits of the several therapeutic agents used.

A PHYSICIAN I should like to ask Dr. Davies to review the dosage of sulfapyridine.

DR. DAVIES I think our dosage is somewhat similar to that employed elsewhere. The initial dose is $\frac{1}{2}$ to $\frac{1}{4}$ gr per pound of body weight. The subsequent maintenance dose for infants is $1\frac{1}{2}$ gr per pound per day in four to six divided doses, and for children 1 gr per pound per day, also in divided doses. In general, we continued the drug about two or three days after the temperature had become normal.

FURTHER STUDIES ON THE PERSONALITY AND SOCIOLOGICAL FACTORS IN THE PROGNOSIS AND TREATMENT OF CHRONIC ALCOHOLISM*

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IN A study reported by us¹ two years ago a preliminary attempt was made to survey systematically the sociological and personality characteristics of 120 alcoholic patients and, in 43 cases where adequate information was available, to determine whether any correlation could be discerned between the personality of an alcoholic patient and the ultimate results of his treatment in a mental hospital of the McLean type. Certain suggestive trends appeared to emerge from this preliminary study. "On the one hand" it was stated, "there is the patient who tends to do well: young (under thirty five years of age), in good physical health, with a history of heavy drinking of less than seven years duration, adaptable, energetic, capable of leadership perhaps egotistical, possibly more attached to his father than to his mother, and in circumstances where a hospital residence of four months or more is feasible. On the other hand there is the patient whose prognosis is poor: older than forty years of age, in poor physical health, a heavy drinker for fifteen years or more, anergic, little ability to adapt himself to new situations, lacking in self confidence, possibly strongly attached to his mother and remaining under treatment for only two and a half months or less. These tentative conclusions seemed sufficiently promising to justify further pursuit of the determinants of prognosis in chronic alcoholic patients treated in a mental hospital.

The present study attempts to find answers or hints of answers to the following two general categories of questions. First, is there an alcoholic type of personality? Are there individuals who are more or less predestined because of some special set of personality or sociologic characteristics to become addicted to the excessive use of alcohol? Current authoritative opinion² would seem to indicate that such is the case. If so, can those characteristics be accurately defined? And secondly, what role can the private mental hospital of the McLean type play in the treatment of chronic alcoholism? Is there a type of alcoholic

patient, possessing this or that set of personality or sociologic traits, to whom the mental hospital offers the best outlook for recovery? If so, what are those favorable prognostic signs and, contrariwise, what are the traits which carry implications of poor prognosis in such a therapeutic setting?

This paper is based on an analysis of the sociological and personality findings in 124 alcoholic patients (100 men, 24 women) the results of whose treatment at McLean Hospital are accurately known. Each of the cases included in this series was selected as satisfying both of the following criteria: the patient's excessive use of alcohol

TABLE 1 Final Hospital Diagnoses in All Cases

	Men	Women
Chronic alcoholism without psychosis	61	14
Chronic alcoholism associated with psychopathic personality	13	3
Chronic alcoholism associated with drug addiction	3	3
Chronic alcoholism associated with pathologic intoxication	2	0
Alcoholic psychosis		
Delirium tremens	4	0
Acute alcoholic hallucinosis	5	1
Manic-depressive psychosis associated with chronic alcoholism	6	1
Paranoid condition associated with chronic alcoholism	1	2
Korotkoff's psychosis	1	0
Other psychoses (cerebral arteriosclerosis, trauma general paresis) associated with chronic alcoholism	4	0
Totals	100	24

was the immediate or principal cause for admission to the hospital, reliable and specific follow-up data were available as to what happened to the patient after his discharge from the hospital with particular regard to the use of alcohol. This information was obtained in most cases by a trained social worker who visited the patient's family and obtained a first-hand contact, often data about a single case were obtained from multiple sources.³

Table 1 indicates the final hospital diagnoses in our 124 cases, 85 of these cases were used in the preliminary study previously mentioned. The 39

It is our experience that the use of questionnaire to obtain follow-up information is wasteful. The percentage of returns is low; the information received is often unreliable and misleading—occasionally quite false—not infrequently the former patient receives receiving questionnaire when, unknown to our surprise, a visit from a tactful and experienced psychiatric social worker will cause no antagonism. In a number of cases carefully worded personal letter to patient living too far away from Boston for visiting elicited the desired information when a questionnaire had brought no response.

*Read at the meeting of the American Psychopathological Association, Atlantic City, New Jersey, June 5, 1939.

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others were selected from the alcoholic patients admitted to McLean Hospital during the last five years, and were known personally to one or both of us during their hospital stay

For the purposes of this presentation the discussion of our material is arranged in the following order: general description of the clinical material including sociologic data, personality traits, psychosexual make-up and drinking habits of the group as a whole, a short discussion of treatment, the results of treatment, conclusions

GENERAL DESCRIPTION OF CLINICAL MATERIAL

Sociological Data

The average age of the 100 male patients was forty, with a range from nineteen to seventy-two. From the standpoint of race, American or English blood predominated, being more than four times as common as the next most frequent racial group (Irish), one unexplained fact was the absence of any Jewish patient in the entire group. Protestants were more numerous than Catholics in the ratio of about 4:1. Fifty-three of the patients were married, 30 single, 11 divorced or separated and 6 widowers. Alcoholism had existed in the immediate family of nearly half the patients: this is a significantly higher incidence of alcoholism than is to be found in the families of the non-alcoholic hospital population. Seventeen of the patients came from families where the use of alcohol was known not to have been a problem. The position of the men patients among siblings revealed no evidence that this factor plays a direct or uniform role in predisposition to alcoholic addiction: 8 were only children, 28 the eldest of two or more siblings, 25 the youngest of two or more siblings, while the rest fell in between the extremes of three or more siblings. Among the married patients 52 had children. Thirty-seven of the male patients were college graduates, 42 were high-school graduates, while the others had received less than a high-school education. Forty-nine of the men were classified as business men, 12 in professions, and 24 unemployed (9 of these were retired), the rest were craftsmen, students, laborers and so forth. With regard to physical status, 69 of the patients were classified as having been in good health, 14 in fair and 17 in poor. In the 31 cases where the physical status was abnormal the high incidence of gastrointestinal and neurologic disturbances was noteworthy.

With regard to the sociologic data of the 24 female patients a number of interesting differences and similarities are to be noted as compared to the men: as remarked in our previous paper, the average admission age (forty-three) was signifi-

cantly higher in the women, the general physical health was poorer and the proportion of college graduates was about a third that of the men, whereas a high-school education was twice as frequent in the non-college women as in the non-college men. The high incidence of familial alcoholism clearly observable in the men was even more striking in the women, being present in every case. There were no single women in the series: 2 were widows, 6 divorced and 16 married.

Personality Traits

In our opinion much doubt is justified as to the psychiatric validity of regarding the human personality as simply a mosaic of character traits—a sort of mysterious and elusive jigsaw puzzle which, when the last pieces have been snugly and neatly tucked into place, presents to the tired but triumphant psychiatrist a clear and composite picture of the individual as a whole. What is here meant by a personality trait is something much more fluid and dynamic: in the course of the careful psychiatric study of each patient, in which an attempt is made to evaluate the current clinical picture in terms of his constitutional endowment and previous experience, there emerge recurring trends, patterns and characteristic modes of adaptive behavior by means of which the individual has attempted again and again to solve his problems and to get along in the world about him and with the other people in it. Are there any such recurring trends or patterns—personality traits—which can be seen, in a fair proportion of the cases, to bear an etiologic relation to the heavy drinking of our alcoholic patients? In so far as we are able to discern the answer is, No. A more variegated collection of personalities and personality types than those of our 124 cases would be difficult to assemble: some were sociable, some seclusive, some stubborn, some easily influenced, some cyclothymic, some schizoid, some intelligent, some dull, and so on *ad infinitum*, the only trait these people seemed to have in common was addiction to the excessive use of alcohol. It is true, as pointed out in our preliminary survey, that many of the men exhibited sociableness and general realistic ability to get along with others, especially at a superficial social level, these traits were striking in 57 patients. Also in 57 patients emotional instability was marked, and definite inferiority feelings were noteworthy in 33. From a careful study of the cases one obtains, however, the impression that these trends reflect secondary developments: that the feelings of inferiority, for example, have in most cases arisen out of situations and circumstances due to the drinking rather

than having been a cause of it. By the time a patient's use of alcohol has become so serious as to necessitate sending him to a mental hospital he has usually been subjected to the several familiar standardized forms of social pressure and sanctions (wives, parents and friends exhortations, threats and so forth) and it is, we believe, these influences, which are secondary to drinking, that are largely responsible for those personality trends which alcoholic patients have been supposed to possess in common. So far as these secondary personality trends are concerned there are no significant differences to be made out between the male and female patients: the absence of inferiority feelings noted among the women of our preliminary study is not borne out in the present series, as in only 5 of the 24 women were such feelings emphasized.

Psychosexual Make-up

In the male patients the sex drive was described as marked in 31 and slight in 19 while only 3 were known to be impotent, the same general percentages held for the women patients. Heterosexual adjustment was considered unsatisfactory in 38 of the men and 15 of the women: overt homosexual tendencies were present in only 9 of the men and in none of the women. In 38 of the men and 17 of the women no homosexual trends latent or overt, could be made out.

Drinking Habits

There seems to be nothing more difficult to evaluate about a group of alcoholic patients than their drinking habits: the greatest variability obtains from patient to patient and even in the same patient at different times. To attempt to generalize seems fruitless. There are two exceptions: it is usually possible to ascertain fairly accurately when a patient first started to use alcohol, and less accurately when his excessive use of alcohol began to be a problem. The average age when drinking first began in our patients was twenty in the men and twenty four in the women: on the other hand, heavy drinking began on the average about ten years later in both sexes—at thirty years with the men and at thirty five with the women. This striking confirmation of the findings in our preliminary study is in accord with our belief that a period of about ten years drinking is required for the vicious circle of drinking to relieve symptoms caused by previous drinking to become established and for true addictive drinking to set in.

TREATMENT

Our concept of the principles of the treatment of chronic alcoholism has been developed and expounded in detail elsewhere;^{1, 2} here it will suffice merely to recapitulate briefly.

It is our conviction that there are two types or stages of drinking, first, symptomatic drinking where the alcohol is taken as the result, or for the relief, of the symptoms of some underlying condition, social, mental or physical, and second addictive drinking—the vicious circle noted above—where the alcohol is taken for the relief of symptoms which have been caused by previous drinking, in a sense, addictive drinking is a later stage or special type of symptomatic drinking where the same agent, alcohol that has caused symptoms is being utilized for their relief. The treatment of symptomatic drinking is simply the treatment of the underlying pathologic condition, whereas the treatment of addictive drinking is much more complicated: it is first of all essential to break up the vicious circle and bring the patient to attain total abstinence, it is then necessary to deal with the original cause of the earlier symptomatic drinking, which not infrequently has been submerged under years of drunkenness and is often not amenable to direct therapeutic attack. Thus, as a rule the problem becomes one of substituting non alcoholic and socially acceptable ways of satisfying a patient's needs and of dealing with his problems.

Each of the patients in this study was removed from his accustomed milieu (often under circumstances of the utmost urgency) and, usually against his will, plunged into the atmosphere of a mental hospital with its regular organized daily routine and, of course, enforced immediate total abstinence. Withdrawal symptoms are treated by non alcoholic means and all the resources of the hospital in hydrotherapy, physical therapy and so forth are brought into play. In the course of the first week a systematic review of the patient's life is instituted, and as the patient's physical condition improves an attempt is made by psychotherapy and re-education to give him intelligent insight into and understanding of the difficulties that have brought him to a mental hospital and to equip him for a lifetime of total abstinence by making available resources other than alcohol for dealing with his problems. In 6 men the orthodox psychoanalytic technique of therapy was attempted, although in no case was a complete analysis possible, the periods during which analysis was carried out varied in the several cases from eight weeks to one year. The average duration of hospital stay was one hundred and nine days for the men and sixty five days for the women.

RESULTS OF TREATMENT

It is possible to divide our 100 alcoholic men and 24 women into three groups depending on the known results of their hospital experiences: first

a group of 15 men and 4 women who have remained abstinent since their discharge from the hospital (with three exceptions the duration has been at least eighteen months), secondly, a group of 36 men and 8 women who while not remaining totally abstinent have nevertheless shown definite improvement and may be considered to have been benefited by the hospital experience, and, thirdly, a group of 49 men and 12 women whose general behavior, particularly with regard to the use of alcohol, has shown no change for the better subsequent to their treatment *

It is immediately apparent on perusal of the sociological data, personality characteristics, psychosexual make-up and drinking habits of each of these three groups of patients that no very striking constant differences exist between them which can be considered as having had prognostic value. The average admission age of each group was about the same in the case of the men—forty years for the abstinent group, forty-two for the improved and thirty-nine for the unimproved, whereas with the women the abstinent group was on the average younger than either the improved or unimproved (forty-one years as contrasted with forty-four for each of the latter). None of the other sociological data—marital state, familial alcoholism, sibling position, religion, education and physical status—showed any constant trends which could be correlated with the outcome.

With regard to the personality traits and psychosexual make-up of the three groups the position is about the same, with the exception that the patients who did well seemed on the whole less sociable and tended to be more unstable emotionally—more easily affected by environmental influences—than did those who did poorly. Also the absence of homosexual trends in the abstinent men may be of significance. It is interesting that the abstinent group began their drinking on the average later than the unimproved group—three and a half years later with the men and seven years later with the women, the evident implications being that the earlier in life drinking starts and the longer it has continued the worse the prognosis. The type of drinking—solitary, periodic, continuous or social—seems to bear no relation to outcome, although the trend, previously remarked, for drinking which at first was periodic and social to become, with the passage of time, continuous and solitary is again apparent.

There is the suggestion that patients who have had previous institutional psychiatric treatment elsewhere do not do so well at McLean Hospital as those who have not had such previous treatment. Also, as noted by other investigators⁴ the presence

of a psychosis, especially delirium, at the time of admission would seem to point in the direction of a more favorable course.

So far as the type of treatment or duration of hospital stay is concerned we are, to our surprise, unable to discern any positive correlation with outcome. The abstinent men had an average hospital residence of one hundred and thirteen days, so did the unimproved group, while for the improved but not cured cases the average duration of hospitalization was one hundred and one days. Similar relations obtained for the women. The 6 men who were exposed to psychoanalytic methods were all unimproved.

It is suggested that the shock many patients experience on finding themselves in a mental hospital is a more potent factor in therapy than one would at first realize, if with this shock come a degree of insight and a realization of the seriousness of their drinking, perhaps one of the most valuable therapeutic contributions the mental hospital has to offer alcoholic patients has been accomplished. This is well shown in one of our female patients who was admitted one day and discharged the next against advice, she was resentful and furious at both her husband and the hospital, yet she has not taken a drink since—almost four years. One wonders if this result could have been improved on had the patient remained a year—or if a prolonged stay might not have tended to remove those very factors which, in her case, seem to have contributed to a favorable outcome. The essential factor here seems to be the clear and dramatic crystallization in the patient's mind of the causal relation between drinking and the critical position in which the patient finds himself (threatened loss of physical or mental integrity). This may be the explanation for the apparent favorable effect of delirium on outcome.

CONCLUSIONS

On the basis of the foregoing findings two main conclusions seem justifiable. First, there does not seem to be any one personality pattern or constellation of personality traits which is typically alcoholic—there is no "alcoholic type", second, the outcome of treatment of chronic alcoholism has little apparent relation to sociological or personality traits, type of therapy or duration of hospital stay.

There are a number of corollaries and subsidiary observations in addition to the foregoing conclusions. In the first place, while there does not seem to be a specific alcoholic type of personality, certain trends—sociability, inferiority feelings and emotional instability—have a high incidence in our group, it is suggested that these traits are secondary to the drinking rather than its cause. Furthermore, the high incidence of alcoholism in

*Eleven of the 124 patients have died since discharge from the hospital.

the families of our alcoholic patients is striking and probably significant. In the second place, there is the suggestion that the period of time during which heavy drinking has existed prior to the beginning of treatment bears a relation to prognosis the earlier in life drinking starts, the poorer the prognosis.

Our general conclusion therefore is that any one—normal, neurotic or psychopathic, manic depressive or schizoid—can become an alcoholic addict if he drinks long enough and heavily

enough (on the average about a decade), and that the younger he is when he starts his drinking, the less likelihood there is for his successful treatment in a mental hospital.

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REPORT ON MEDICAL PROGRESS

ORTHOPEDIC SURGERY

M. N. SMITH PETERSEN, M.D.*

BOSTON

THIS report is in no way intended to cover all that is new in diagnostic measures, clinical entities and methods of treatment; its purpose is to point out those advances that are still in the experimental stage, and to make suggestions which may be productive of a better understanding of orthopedic problems.

Correct diagnosis is the foundation for correct treatment leading to relief of pain and often to cure of the condition for which the patient seeks advice. It becomes all important, then, that we so conduct our examinations that we can have faith in the conclusions and the diagnosis based on them. In order to accomplish this we must interpret every symptom, every sign, and not be content to go through a routine examination without rationalization.

Pain is probably the most important source of information we have, yet it is one of the most neglected. There are so many types of pain that it is difficult to enumerate them. The chief cause of pain is the tension of structures; as soon as the tension is relieved the pain subsides; a ruptured appendix is a good example. The reaction to a lesion, then, is swelling with tension causing what is referred to as local pain. Because of the innervation of the structures involved the brain refers the pain along the peripheral distribution of the nerves of the affected region; this gives rise to so-called referred pain. This is still primary pain since it is the direct result of the lesion. So as to protect the region involved the muscles go into spasm which is constant and therefore puts the muscles under unusual strain rendering their attachments sensitive and painful. This

type of pain may be referred to as secondary or protective. By analyzing an apparently complex picture of pain in terms of primary and secondary pain, the problem very often becomes simplified and instead of ones saying that the patient is a neurotic and has pain everywhere, a reasonable explanation may be found.

The above refers particularly to preoperative conditions. Postoperatively we also have various types of pain that should be interpreted and properly evaluated. Any surgical procedure results in local pain, discomfort or soreness, a surgical procedure on the spine or on the extremities necessarily demands a certain period of partial or complete immobilization with inevitable and sometimes very striking muscle and bone atrophy.

When functional treatment is started there is necessarily a certain amount of protective muscle spasm, with accompanying tenderness over muscle attachments. We also have the discomforts secondary to the mobilization of the joints involved; these are common complaints, usually properly treated. One type of pain often unrecognized is that due to bone atrophy, the atrophy in itself is not painful but it is accompanied by circulatory stasis aggravated by faulty muscular function. Unless care is taken to relieve this bone congestion by various means, such as elevation and proper exercises, the pain may occasionally be severe enough to interfere with function and a vicious circle is established. Conditions of this type are extremely difficult to treat, and if routine measures are prescribed results will not be obtained; the treatment must aim to relieve congestion. Interpretation of pain, then, must be our guiding principle in prescribing treatment, and we shall succeed better if we pay more attention to it.

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"Sciatica" is a term which has always been and still is misused, in general it is applied to severe, sometimes disabling pain in the lower extremities. If this term is used it should always be accompanied by an accurate description of the distribution of the pain as pointed out by the patient. The commonest distribution to which this term is applied is that over the posterior aspect of the thigh and posterior and posterolateral calf, and sometimes the lateral border of the foot. This corresponds to the peripheral distribution of the first and second sacral nerves. Until a few years ago it was accounted for on the basis of neuritis, fasciitis and myositis. Then came a period when it was commonly associated with lesions involving the sacroiliac joint. There was good reason for this interpretation, since tuberculosis of this joint is commonly accompanied by this distribution of pain. I am one of those who for years claimed that sacroiliac lesions alone could logically account for it. With the advent of ruptures of the intervertebral disk, another entity accounting for this distribution of pain was added.

The neurologists have as yet not furnished us with a satisfactory explanation of the mechanism productive of this distribution of pain, nor have they told us why lesions of the third, fourth and fifth lumbar intervertebral disks should produce a distribution of pain so very nearly the same. Unquestionably the distribution is only apparently the same, and if we are accurate in recording the patient's statements, we may some day be able to point out variations depending on the particular disk involved. This will never be achieved if we persist in describing pain referred to the lower extremity by the term "sciatica."

Rupture of the intervertebral disk is a distinct clinical entity, about this there can be no argument. It unquestionably accounts for many cases of chronic back pain unsuccessfully treated in the past. On the other hand, many patients suffering from this condition must have been relieved by spinal fusions, even though the real underlying cause was not recognized. The recognition of this lesion has meant definite progress, not only in treating patients presenting it but also in the study of chronic disabling back conditions.

The orthopedic surgeon is no longer going to be content to treat patients with chronic back pain, accompanied by referred pain to the lower extremities, by back braces and plaster casts for any length of time, he is going to institute early neurological examination, accompanied by a lumbar puncture, thereby avoiding delay in recognizing intraspinal conditions. As a matter of fact, the orthopedic surgeon now rarely examines a patient complaining of back pain without testing

the reflexes—something which unfortunately was rarely done before the importance of injuries to intervertebral disks was recognized. On the other hand, the neurologist and neurological surgeon would never consider the examination of a patient complaining of pain referred to the lower extremities as complete without performing the test of straight leg-raising. Thus far they have confined themselves to this one orthopedic test, but even so it denotes progress.

It is interesting to note that no satisfactory explanation as to the mechanism of pain production by straight leg-raising has been furnished by either the neurologist or the orthopedic surgeon. Orthopedically the test was supposed to bring about a tightness of the hamstrings, resulting in strain or tension's being transmitted to the sacroiliac ligaments, thereby producing pain. When the pain did not come on until the lumbar spine moved, the test was considered as pointing toward a lumbar lesion. The fact remains, however, that in cases of pain referred to the lower extremity secondary to a lesion of the intervertebral disk, straight leg-raising is productive of pain before the hamstrings become taut and before the lumbar spine moves, at least this is a very common observation. My interpretation of this phenomenon is that raising the lower extremity with the knee straight, particularly if the foot is kept in dorsiflexion, brings about tension of the gastrocnemius and the hamstrings. Since these structures are hypersensitive the tension aggravates the pain. This explanation, however, may not be satisfactory to the neurologist.

Any new clinical entity, any new method of treatment, is apt to be followed by a wave of hyperenthusiasm, as experience is gained the pendulum tends to swing back, and we encounter a period of increasing conservatism. This period has already set in as regards intervertebral disk injuries and their treatment, Lipiodol is no longer used as extensively as it was, since we now recognize that it is not so innocent and inert as at first supposed. Air injections are beginning to take the place of Lipiodol, which is used only when absolutely necessary.

Arthritis cannot properly be referred to as a new clinical entity, but there are certain aspects of the diagnosis and treatment of this condition which have been developed in recent years, and which should be referred to as relatively new and distinctly helpful. The treatment of this condition has gone through cycles of enthusiasm—vaccines, diets of various types, as well as different forms of physiotherapy. At present there is a tendency to adopt a more analytical attitude, evaluating these different types of treatment and possibly favoring

good general hygiene, some special form of therapy if indicated, and attention to the local condition of the joints. The sedimentation rate has proved of distinct value in judging the activity of the disease and the response to various forms of therapy. I believe that this particular test has been effective in evaluating the different specific forms of treatment and thereby has led to the present somewhat conservative attitude.

Hypertrophic arthritis is more commonly referred to as "degenerative joint disease" this is quite proper but even this term leaves something to be desired. In the last analysis the condition should be referred to as degenerative joint changes, secondary to wear and tear. It is not a disease process it is a physiologic process secondary to advance in age. If we keep this in mind we shall be less apt to subject a patient to elimination of foci of infection which rarely bear any relation to the joint changes, we shall be more apt to look for mechanical reasons for the abnormal wear and tear and try to eliminate these by correction of mechanics.

A recent development in the surgical treatment of arthritis is encouraging. In the past arthroplasty by means of an interposed perishable membrane has been successful in a comparatively small percentage of cases. This procedure could never be undertaken during the active stage of rheumatoid arthritis, if it was it invariably led to failure. The new form of arthroplasty is based on the principle of interposing a permanent mold by which Nature can do her repair work. This mold is made of an inert metal which will not give rise to excessive scar formation and relaxation of the joint. By insertion of such a mold even during the acute or active stage of the disease pain is diminished and function improved. The procedure has as yet not stood the test of time, our attitude must therefore be conservative. Surgery of this type should be carried out in selected cases only, and chiefly for the relief of pain without expecting too great an improvement in function. In cases of degenerative joint disease particularly when the hip joint is involved the results are much more encouraging both as concerns relief of pain and improvement in function.

In relation to the joint, joint changes and joint mechanics, we must keep in mind the innumerable bursae found wherever there is friction on tension. The subdeltoid is the classic example of a bursa apt to give rise to symptoms because of excessive abnormal function of the shoulder. We must not lose sight of bursitis as a frequent cause of local acute pain wherever we have muscles gliding over a bony prominence. Pain over the radial head (tennis elbow) unilateral cervical

pain, pain in relation to the superior and inferior angles of the scapula, localized pain in relation to the transverse processes of the lumbar spine, particularly the third, acute pain just above the middle of Poupart's ligament (iliopectineal bursitis), pain over the greater femoral trochanter and pain in numberless other regions can very often be accounted for on the basis of bursitis. Injection of normal saline under novocain anesthesia is very effective in the treatment of bursitis and is gradually taking the place of open surgery even when the x ray film shows calcium deposits.

The treatment of osteomyelitis is entering a new phase in so far as more attention is being paid to its bacteriological aspect the patient's general physical condition is considered first surgical treatment and local condition second. Before the patient is subjected to surgical treatment the possibility of chemotherapy is duly weighed. Because of the increasing importance of the bacteriological aspect, we find here and there surgeons who have gained a wide knowledge of bacteriology and are therefore qualified to deal with the surgery of septic conditions. This is distinct progress and will lead to infinitely better understanding of the conditions underlying osteomyelitis.

There is an increasing demand for the services of the orthopedic surgeon in the treatment of fractures. This is natural since his specialty brings him into constant contact with joint function and the problems involved. After all, the treatment of fractures depends on a knowledge of the neighboring joints which the general surgeon cannot be expected to possess. Consequently it seems fair to say a word about the progress in the treatment of two fractures,—those of the spine and of the neck of the femur,—progress for which orthopedic surgeons have been responsible.

Fractures of the spine until recent years were left without correction this commonly gave rise to faulty joint function with resulting partial or complete disability. The correction of fractures of the vertebral bodies has returned a large number of these patients to their pre injury occupations.

Fracture of the neck of the femur has always been a difficult problem and consequently has been referred to as the unsolved fracture. Internal fixation of this fracture has led to a saving of many lives, eliminated much of the pain and achieved bony union with good function in as high a percentage of cases as in fractures into other joints.

The increasing tendency in the treatment of congenital deformities is to guide growth gradually rather than to correct deformities immediately. This is logical treatment since immediate correction by open surgery commonly leads to inter

ference with growth, thus causing secondary deformities

Opinion as to the treatment of tuberculosis of bones and joints is still divided. It is fair to say that surgical treatment is gaining in favor, since it provides the patient with a permanent internal protection against recurrence. If surgical treatment is undertaken during the period of growth, this should never be done until the patient is in the optimum physical condition, and surgery should be performed in such a way as to cause the minimum interference with growth. The arguments of those who favor conservative non-operative treatment are based on less interference with growth, less

chance of secondary foci, scientific support of the arguments is lacking.

No startling discoveries in the treatment of poliomyelitis have been made in recent years. Excellent advice on the treatment of the acute stage can be found in current articles. Treatment during the later stages consists in correction of deformities which have developed in spite of good treatment or because of faulty treatment, such measures consist chiefly in arthrodesis of joints. Muscle transplantation, which may be referred to as treatment aiming to compensate for paralysis, is becoming simplified and therefore increasingly efficient.

264 Beacon Street.

CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTHEMORTAL AND POSTMORTAL RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., Editor

CASE 25451

PRESENTATION OF CASE

A forty-two-year-old ex-sailor, ex soldier, ex prize fighter and salesman was admitted to the hospital complaining of jaundice of about five weeks duration.

Eighteen years before admission the patient developed a chancre and a year later suffered from *iritis*. He then consulted a physician who diagnosed syphilis. Over the following ten year period he received at least forty-eight injections of neocarsphenamine or sulfarsphenamine twenty injections of tryparsamide and one hundred and five of bismuth. Potassium iodide and mercury were taken by mouth. For the seven year period prior to admission he received no antisyphilitic therapy. Three lumbar punctures performed thirteen, twelve and eleven years before entry gave spinal fluid total proteins ranging from 59 to 66 mg per 100 cc. and negative Wassermann tests. However blood Hinton tests were persistently positive and Wassermann tests occasionally negative. These data were obtained from the patient's outpatient records, which also showed that no central nervous symptoms had ever been elicited. About four and a half months before entry he noticed marked anorexia and that his urine was becoming increasingly brown. Approximately five weeks before entry his eyes became yellow. He had had no weight loss, nausea or vomiting, nor had he noticed any clay-colored or tarry stools.

For many years he had drunk from one to two pints of hard liquor a day and his eyes had been intermittently "yellow" for fifteen years before admission. For a long while the patient had had crusting in the nasal passages with bleeding when he forcefully blew his nose. His family history was not contributory.

The physical examination revealed a well developed and well nourished flushed icteric, nervous man, who did not appear acutely ill. His speech was slow, and there was a tremor of the hands and jaw. The nasal mucous membranes were atrophic and crusted, the tongue tremulous. Examination of the lungs was normal. The heart was not enlarged. There was a loud short sys-

tolic murmur heard in the second left intercostal space and transmitted well into the great vessels of the right neck. The blood pressure was 144 systolic, 80 diastolic. The liver was percussed at the level of the fifth rib anteriorly and was felt as a mass without gross nodularity two finger breadths below the costal margin. The spleen was palpated two to three fingerbreadths below the costal margin. There was slight shifting abdominal dullness. Examination of the rectum revealed internal hemorrhoids. Slight pitting edema was noted around the ankles.

The temperature was 101°F., the pulse 90, and the respirations 22.

Examinations of the urine showed specific gravities ranging from 1.010 to 1.022, albumin from 0 to ++ and no sugar, bile varied from 0 to +, the sediments contained innumerable red cells, and the white cells varied from 10 to many per high-power field, there were no casts. The blood examinations revealed red counts from 2,600,000 to 3,500,000 with 60 per cent hemoglobin, and white-cell counts from 4700 to 5400 with 66 per cent polymorphonuclears. The stools were brown and guaiac negative. The blood Hinton test was positive and the Wassermann weakly positive. The serum protein was 6.4 to 7.4 gm per 100 cc., the van den Bergh 3.9 mg. A bromsul falcin liver test showed 45 per cent dye retention. The Takata Ara test was strongly positive, and the formal gel test positive after forty-eight hours. A lumbar puncture revealed normal dynamics with a slightly icteric fluid which had a total protein of 30 mg per 100 cc. The spinal fluid Wassermann test was negative. The gold-sol curve read 0.012210000. Abdominal paracenteses yielded 1600 and 3000 cc. of clear yellow transudate, which showed no tumor cells.

X-ray studies of the esophagus revealed extensive varices. A chest plate showed the diaphragms in a high position with the heart slightly enlarged but without characteristic configuration. The lung fields were clear.

The patient ran a slow but steady downhill course. He spiked a daily temperature up to 103°F. The pulse varied between 80 and 120. He was treated intensively with potassium iodide, vitamins, transfusions and a high-carbohydrate diet. However he progressively became more jaundiced, mentally dull and confused. On two occasions he vomited several ounces of blood. He died on the twenty-ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. CHARLES L. SHORT Will you show the films, Dr. Holmes?

DR. GEORGE W. HOLMES One of the charac-

teristics of esophageal varices is that they are not present in all films at all times. For instance of these three films on the screen the first and third are suggestive but not definitely characteristic, whereas the findings in the middle film justify a positive statement that varices are present. The heart shows surprisingly little—certainly no evidence of disease of the great vessels. It is questionable whether there is any disease of the heart at all.

DR SHORT: Have there been any exceptions to the rule that if you find varices you can make a diagnosis of portal obstruction—excluding this case of course?

DR HOLMES: Dr Schatzki has reported one or two cases of congenital anomalies. We had one case where a picture indistinguishable from varices was produced by something entirely different. However, I think that in the majority of cases this picture means portal obstruction.

DR SHORT: Would you be willing to predict how long the portal obstruction has been present from the extent of the varices, or is that impossible?

DR HOLMES: It is impossible.

DR SHORT: In view not only of the varices but also of the other findings, I think we can accept as a fact that this patient had liver disease with portal obstruction. There was jaundice, an enlarged liver and spleen, ascites, evidence of impaired liver function and, finally and probably of most importance, demonstration of the varices. I think we can also assume that the patient died of liver insufficiency. The fever can be explained on that basis, and we have no evidence of any intercurrent infection. The rather loud systolic murmur could be accounted for by his anemia, and with the negative chest x-ray film I do not believe we have to make a diagnosis of heart disease. The anemia with a rather low white-cell count is quite characteristically found in disease of the liver. We do not have to assume that he had had hemorrhages.

The only point in the story that is difficult to bring in is the constant finding of large quantities of red cells in the urine, along with some white cells. That tends to make you think of some complicating condition,—possibly bacterial endocarditis with renal infarcts,—but again there is no positive evidence, and we shall either have to call the hematuria an unimportant coincidental finding or pin it on the hemorrhagic tendency which is present in liver disease. Evidently the service accepted it this way because no further investigations were carried out, unless perhaps they were not done because the patient was too sick.

I shall assume then that this patient died of liver

insufficiency alone. Next, the more difficult question comes up as to what was the cause or the causes of the liver disease. He had, as you remember, a large amount of antisiphilic treatment including arsphenamine, which is most important in causing liver damage. He evidently was observed in the Out Patient Department, and there is no history of his having had jaundice while under treatment with arsphenamine. It is possible that he had subclinical latent damage to the liver developing in the course of the treatment, but that is impossible to prove, and the fact that he had had a ten-year interval without any anti-syphilitic treatment vitiates the possibility that anti-syphilitic drugs played a role. Next, we have to try to find out what part syphilis played in this case. Of course, syphilis may be a factor in any type of liver disease, on the other hand, at autopsy any patient with syphilis may show scars in his liver and have had no symptoms during life. Then there are cases reported of typical portal cirrhosis which were apparently due to syphilis. But that is a rather rare condition, and very difficult to prove, I believe, during the patient's life. Even if the therapeutic test fails, I do not believe we can rule out syphilis as a possible cause of portal cirrhosis in a patient with this disease. But in view of the comparative rarity of this condition, and the fact that he was quite adequately treated for syphilis, I shall dismiss the possibility of syphilis as a cause for the acute liver damage, although I think it is not improbable that some scars may be found by Dr Mallory in the liver, representing healed gummas.

We are left then with the ordinary type of portal cirrhosis, in which we know alcohol is a factor. We cannot say from the varices that the process was of long standing, but it may well have been so in an asymptomatic form. The only symptoms he had until five months before admission were occasional yellowing of the eyes and nosebleeds, and neither of them may have been really significant. I think it is more logical to believe that he had a portal cirrhosis of long standing and that he died with what is called an acutely decompensated liver. The question is whether the final episode was of the nature of an acute necrosis of the liver or simply an exacerbation of the portal cirrhosis. He had a rather low van den Bergh test and only a moderately impaired liver function when he came in, but of course he was not acutely ill at that time. We do not know what the tests showed later on, but from the picture here and from the duration of the terminal course, I should say that simple portal cirrhosis with an exacerbation could account for his death without bringing in acute liver necrosis. So I should expect to find

at autopsy a long standing fibrotic process resembling portal cirrhosis, and perhaps some evidence of activity of this disease in the liver cells.

In any case of liver disease with a rapid, downhill course we have to think of two possible complications. One is the development of a primary hepatoma of the liver. There is no positive evidence of that in the form either of a palpable tumor or of one demonstrable by x-ray. There is no evidence of metastases, so I do not believe we can make that diagnosis although we always have to keep it in mind. The second possibility is portal thrombosis shortly before death. Again we cannot prove that, and the diagnosis is not often made in life. He apparently did not have a sudden increase in ascites, so we shall have to say there is no proof that he had portal thrombosis.

In conclusion I think this patient died in an acute exacerbation of an alcoholic or portal cirrhosis, with a liver that may show some scars of old gummas.

DR. TRACY B. MALLORY: Are there any other suggestions?

DR. WILLIAM B. BREED: I should like to ask Dr. Holmes, in view of what Dr. Short suggested about hepatoma, whether that angle in the right diaphragm means any more to him.

DR. HOLMES: No, I think it is well within normal limits for his build.

DR. PAUL S. HANSEN: When he was on the wards he had a positive Wassermann test and had had negative tests in the past. We wondered if that indicated active visceral syphilis. As for the hematuria we did not ignore it. He had a negative intravenous pyelogram, and we wondered whether the hematuria might represent a defect in the blood-clotting mechanism or possibly a varix in the kidney. We could not explain a varix anatomically but thought there might be an associated thrombosis or partial occlusion of the renal vein.

DR. MALLORY: I remember having been asked to see this patient on the ward with regard to the question as to whether syphilis played any part in his liver disease. I was particularly impressed by an almost lyrical description which he gave me of an *estaminet* just back of the lines in France in 1918 which specialized on Demerol so I think he was already a chronic alcoholic even during the last war, when he was a fairly young man. At that time I expressed the opinion that syphilis would be found to have nothing to do with his hepatic insufficiency and I am still of that opinion after the autopsy.

CLINICAL DIAGNOSES

Cirrhosis of liver (? portal ? luetic)
Acute hepatitis
Esophageal varices
Serological lues

DR. SHORT'S DIAGNOSES

Portal (alcoholic) cirrhosis, decompensated
Healed gummas of the liver?

ANATOMICAL DIAGNOSES

Cirrhosis of liver alcoholic.
Esophageal varices.
Jaundice
Ascites
Bronchopneumonia localized, right upper lobe.
Perisplenitis
Pulmonary tuberculosis, left apex healed, fibrous
Operative scars herniorrhaphy, right abdominal paracentesis
Hemorrhage into gastrointestinal tract.

PATHOLOGICAL DISCUSSION

DR. MALLORY: He had what we pathologists always call a hobnail liver. I formerly had the impression that that was a very descriptive term but after trying it out for several years on medical students I began to wonder about it. Apparently present-day medical students have never seen hobnails. I asked what size hobnails are and got answers varying from 1 up to 35 mm in diameter.

This particular liver showed very uniform nodules varying from 2 to 3 mm in diameter. It was still a little larger than normal weighing 1800 gm. We know that patients with alcoholic cirrhosis go through a stage in which the liver is greatly enlarged—sometimes up to 4000 or 5000 gm. This had shrunk considerably from that stage but was still at the upper limit of normal. The esophageal varices were very extensive, and there was no doubt about them anatomically. The spleen, as you would expect with portal obstruction was considerably enlarged weighing 600 gm., and showed early stages of the characteristic fibrotic changes that you get with long standing portal obstruction. It is worth emphasizing that during life the leukopenia which is characteristically found with chronic portal obstruction was present. I am strongly of the opinion that this finding is due to passive congestion of the spleen because it disappears with splenectomy whether or not the patient has cirrhosis makes no difference. Following splenectomy the

white count will run around 10,000 as long as the patient lives. We found nothing to account for the hematuria. Our only guess is that it must have been a manifestation of a purpuric tendency. There were red cells found in the convoluted tubules but there was no significant glomerular damage to account for it.

DR. SHORT: Was there any evidence of activity in the liver cells?

DR. MALLORY: There was no significant evidence of recent degeneration. I should have to assume it was just a liver that had been running along on a low reserve and suddenly became decompensated. There was no anatomical evidence of syphilis even despite a complete examination of the central nervous system.

CASE 25452

PRESENTATION OF CASE

A fifty-two-year-old, white married woolen-mill foreman was admitted complaining of weakness following a massive hemorrhage by rectum and fainting two weeks before entry.

About four and a half months before admission the patient noted a gradual onset of gastrointestinal disturbances with alternating constipation and mild diarrhea. For a month laxatives gave moderate relief. He began to lose weight, became anorexic and weak and suffered "indigestion," with variable amounts of gaseous distention. A number of bad teeth were pulled about three weeks before entry. Several days later he had a sudden massive hemorrhage by rectum, consisting of large amounts of bright-red blood, and subsequently passed black stools. He was brought to an outside hospital in shock. The systolic blood pressure was 50. In the hospital he continued to show traces of blood in the stools for several days. After this had ceased and a number of transfusions had been given, a barium enema was done, which showed a large dilated rectum and a slowly filling colon. There was an irregular area in the sigmoid suggestive of carcinoma. His anemia responded well to the transfusions, but he remained toxic and ran a septic type of temperature for several days. The red-blood-cell count was 3,150,000 two days before entry, and the patient felt much better. He was then brought to this hospital for further treatment.

His past and family histories were noncontributory.

Physical examination showed a pale man who evidently had lost weight. He had no teeth. His pharynx was somewhat injected. No peripheral lymph nodes were noted. Examination of the lungs was negative. The heart was negative. The

blood pressure was 98 systolic, 60 diastolic. The abdomen was soft and slightly distended. Peristalsis was active, and there was no tenderness or spasm. In the epigastrium there was a questionable mass, possibly the left lobe of the liver. The extremities were negative. A neurological examination was negative.

The temperature was 99°F, the pulse 82, and the respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 3,980,000 with a hemoglobin of 65 per cent, and a white-cell count of 5400 with 75 per cent polymorphonuclears. The nonprotein nitrogen of the serum was 20 mg per 100 cc, and the protein 5.1 gm, the chlorides were equivalent to 92 cc of N/10 sodium chloride. A blood Hinton test was negative.

X-ray films of the chest revealed multiple discrete areas of soft hazy density scattered throughout both lung fields. The hilus shadows were a little prominent on both sides and slightly lobulated. A barium enema passed without interruption to the cecum, and no constant defects were demonstrated. Two days later this was repeated. The colon was empty and well visualized. It showed no defects, and the terminal ileum was not remarkable. A gastrointestinal series showed the stomach to be elongated and displaced to the left, though it showed no defects. The first portion of the duodenum filled readily and showed pressure defects on its superior margin; there was a similar rounded defect on the superior margin of the second portion. At six hours the stomach was empty and the motor meal lay in the terminal ileum and proximal colon. The hepatic flexure was displaced downward and medially. There was no evidence of intrinsic disease in the upper gastrointestinal tract, but there was evidence of marked enlargement of the liver.

On the thirteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD L. YOUNG: The history of this case certainly gives us little to go on. There had been only four months of rather vague intestinal symptoms which do not point to any specific portion of the gastrointestinal tract, and there was one massive hemorrhage which might have come from any point from the esophagus downward. We inevitably turn for help to the radiologist and we read of a suggestion of something that displaced the stomach and the hepatic flexure and slightly deformed the duodenum, apparently by external pressure. Dr. Hampton, can you help us out before we begin to do what guessing we can?

DR. AUBREY O. HAMPTON: We found no varices

or enlargement of the spleen but fairly definite evidence of enlargement of the liver. I think the pressure defects in the duodenum represent pressure from the liver or gall bladder. The first one described is at the beginning of the second portion of the duodenum. That might be attributed either to gall bladder or liver. It is in the area of each. The examination of the colon in the hospital appeared normal but on this film at another examination there was something that suggested spasm or certainly a transitory defect in the sigmoid. We have seen such spasm with diverticulitis and extrinsic cancer. It is not the picture of intrinsic disease. On the chest plate here are definite round nodules scattered through the lung. I say "definite," though they are not easily seen at first glance, they are there, nevertheless, and they average about 1 cm in diameter. There also are irregular dense lines running toward the lung root on the right side.

DR. CHESTER M. JONES: Is that picture enough to make you fairly certain they are metastases, or does it only make you suspicious?

DR. HAMPTON: I think we should be quite certain.

DR. YOUNG: Is it true that a posterior wall ulcer of the duodenum or esophageal varices might be missed in x-ray examination?

DR. HAMPTON: Yes. We have missed both of them.

DR. YOUNG: In spite of my question to Dr. Hampton, the whole picture seems to be against esophageal varices and posterior wall ulcer although either might produce hemorrhage. Even very acute gastritis has been reported as the cause of massive hemorrhage. The other conditions that cause bleeding so seldom cause a massive hemorrhage of this type that I think we can throw them out. There were black stools so that almost certainly the hemorrhage came from a lesion higher than the one first suspected, that is, a sigmoidal carcinoma. It would seem to me that the evidence points toward the upper gastrointestinal tract. The slight temperature, the loss of weight, the evidence of scattered pulmonary lesions by x-ray make cancer the most probable diagnosis and the lesion must have involved the gastrointestinal tract. The only way in which I can fit all the facts together is to make a diagnosis of retroperitoneal malignant tumor that has involved the bowel. I am reminded of a case that I saw at autopsy here some time ago of retroperitoneal sarcoma that had ulcerated through the duodenum and resulted in a massive hemorrhage which was the cause of death. I do not know where else to place the primary lesion. Of course this pressure defect and the fact that

this epigastric mass felt like the liver make me wonder if there are actually an atypical type of portal obstruction and portal cirrhosis with esophageal varices, but I am going to put that far down the line and make cancer outside the gastrointestinal tract and ulcerating into it as my first bet.

DR. WILLIAM B. BREED: On the evidence of the record, what were the indications for exploration in this case?

DR. YOUNG: The fact that nobody knew what was the matter and the wild chance that something might be discovered that would help him. In answer to the question as to whether he advised operation following a diagnosis of cancer of the head of the pancreas, Dr. Fred Shattuck used to say "Yes, because of the fallibility of human diagnosis." I think there may have been some condition present which could have been helped surgically, and in any case I should have operated to establish a diagnosis because if it were retroperitoneal lymphoma a considerable degree of relief might be obtained with radiation therapy.

DR. BREED: I was wondering whether one could accept the x-ray evidence of metastases to the lungs. That might influence you somewhat in exploration.

DR. YOUNG: I practically forced Dr. Hampton to say yes.

DR. HAMPTON: I went on probabilities, about nine out of ten.

DR. BREED: Would the presence or absence of neoplastic nodules in the lungs make any difference in your decision to operate?

DR. YOUNG: If I were sure the lungs were filled with carcinoma of course I should not operate.

DR. J. H. MEANS: The thing that bothers me is that I cannot find any record of the rectal examination, but I suppose it was done. I do not believe that disease in the rectum has been ruled out, even though it is a little strange to have a massive hemorrhage from a rectal cancer.

DR. YOUNG: Did you ever see one give tarry stools?

DR. MEANS: They may be black from some other reason. I think he should have had a rectal examination.

DR. MARSHALL K. BARTLETT: Both rectal examination and proctoscopy were done, and both were negative.

DR. YOUNG: I have never seen a carcinoma of the large bowel that resulted in tarry stools or a massive, nearly fatal hemorrhage.

DR. MEANS: Nor have I.

DR. LELAND S. MCKITTRICK: I have seen a carcinoma of the rectum that gave massive hemor-

rhage, the blood going up as well as down, and then the patient had dark stools afterward. Furthermore, I have seen patients explored for massive hemorrhage and nothing found.

DR TRACY B MALLORY: Do you wish to tell the operative findings, Dr Bartlett?

DR BARTLETT: The colon was entirely normal, also the stomach and duodenum. About two thirds of the way down the small bowel was a segment about 60 cm in length that was abnormal. In this segment multiple areas of thickening of the wall 1 or 2 cm in width were found which tended to encircle the lumen of the bowel. The thickenings were soft and did not feel like carcinoma. About 180 cm of small bowel was resected.

DR MALLORY: What was your preoperative diagnosis?

DR BARTLETT: I believe we guessed carcinoma of the gall bladder, but we certainly were not very sure about it.

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Carcinoma at head of pancreas or of gall bladder

DR YOUNG'S DIAGNOSIS

Retroperitoneal malignancy involving the small intestine

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Lymphoblastoma, Hodgkin's type, with involvement of ileum, lung, liver, spleen, adrenals and thyroid

Septicemia (*Bacillus coli*)

Pulmonary infarct, left lower lobe

Hydrothorax, serosanguineous, bilateral

Pulmonary edema, marked

Operative wound: resection of segment of ileum

PATHOLOGICAL DISCUSSION

DR MALLORY: The lesions of the small intestine proved to be shallow ulcers with slightly indurated margins. It was quite obvious that they represented malignant tumor, but it was not too evident what the type was. Fortunately, however, a biopsy was taken of a metastatic nodule of the liver and on that it was perfectly clear that we were dealing with Hodgkin's disease. The patient died rather suddenly a few days after operation and came to autopsy. We found many Hodgkin's nodules throughout the liver and a few in the spleen, with considerable involvement of the retroperitoneal nodes and multiple lesions throughout the lungs. There was a terminal pulmonary embolus which was at least in part, if not wholly, re-

sponsible for his death. If this patient had survived the operation and then had x-ray treatment, it is quite likely his life might have been prolonged for some time.

DR McKITTRICK: Is it common for Hodgkin's disease to give discrete nodules within the lung such as this man had?

DR MALLORY: It is not particularly common but does occur. That is the one form of lymphoma that does involve the lung with significant frequency. Hodgkin's disease can on occasion simulate tuberculosis of the lungs in every respect or look, as this case did, like metastatic cancer.

DR MEANS: If you took a series of cases of cancer of the small bowel, have you any idea what percentage would be due to lymphoma?

DR MALLORY: I rather think over half.

DR JONES: Was the liver as large as it seems to be on the x-ray plate?

DR MALLORY: It weighed 2100 gm, which is large but not tremendously so.

DR JONES: Would that account for the pressure defects in the duodenum?

DR HAMPTON: I think that they were probably due to gall bladder.

DR MALLORY: Dr Hampton, if you had been asked to look specifically for a lesion in the small bowel, would you have found it?

DR HAMPTON: I doubt it. These lesions are hard enough to find in the stomach, and if there is not a large mass of ulcerative tumor, we usually miss it.

DR MEANS: What was the actual source of the blood?

DR MALLORY: It was not determined in this case. In the majority of stomach cases with massive hemorrhage one can find erosion of a major vessel. We have not had much luck finding the source of hemorrhage with tumors lower down—below the duodenum, I should say.

DR JONES: There was one curious laboratory finding of interest. After a good deal of bleeding the patient had a white-cell count of 5400. That is unusual and suggests the possibility of intrahepatic disease. It is characteristic of primary liver disease, and I think that Dr Frank Hunter has told me of cases with just this picture that had a good deal of diffuse infiltration of the liver with lymphomatous tissue.

DR MALLORY: We made a number of sections of the bone marrow, thinking the blood picture could be explained on bone-marrow metastases. We found no evidence of Hodgkin's disease, but there was a marked hyperplasia of red cells and marked aplasia of white cells, a picture almost suggesting mild agranulocytosis.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
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THE NEW HAMPSHIRE MEDICAL SOCIETY
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SUBSCRIPTION TERMS: \$6.00 per year in advance, postage paid, for the United States; Canada, \$7.00 per year; \$9.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received or later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway Boston, Massachusetts.

BLUE CROSS BENEFITS

A LETTER published in this issue of the *Journal* calls attention to the changes in benefits provided by the Associated Hospital Service Corporation of Massachusetts that have been necessitated in order to ensure future stability of the organization and hence, to protect the interests of all participants. Chief blame for these changes is placed on abuses practiced by both subscribers and physicians. Most of these have been apparently due to a misunderstanding in regard to just what is provided by a Blue Cross membership. This is being cleared up and recent figures show that the great majority of subscribers and physicians, particularly the latter are adjusting themselves to the letter and spirit of the contracts as soon as they thoroughly understand them. An example of this is the distinct cutting down on the part of physicians in sending subscribers to hospitals under non-emergency con-

ditions for diagnostic purposes or periodic health examinations, neither of which is included in the contract.

An appreciable number of patients are still remaining extra days in hospitals at the expense of the Blue Cross. In some cases this has occurred after the physicians have said that the patients could be discharged, and in other cases the physicians, because the Blue Cross was paying the bills, have not encouraged the patients to leave the hospital as soon as they would those patients who were paying their own way. The subscriber's contract is so arranged that if the subscriber stays in the hospital after the physician recommends discharge the bill is supposed to be borne by the patient.

It seems only reasonable that subscribers should abide by the terms of their contracts and that physicians should treat Blue Cross members in the same way that they treat other patients. In this way an unfair financial burden will not be placed on the Blue Cross and any additional reductions in benefits will probably be avoided.

A NEW OPERATION FOR TRIGEMINAL NEURALGIA

NEURALGIA of the face of a paroxysmal and severe type has been known from the very earliest times of medicine. A precise description of this disease was not given, however, until 1776, by John Fothergill. As medicinal treatment failed trigeminal neuralgia was one of the first neurological conditions to be attacked by the surgeon. At first the peripheral nerves were evulsed only to find that they grew back promptly and the pain returned within a few weeks or months. Next the gasserian ganglion itself was excised, a marked step in progress, for this removed the pain permanently and, for the first time, relief was given for one of the most serious diseases in medicine. In the days before the gasserian ganglion operation many patients were known to have committed suicide rather than tolerate the repeated attacks of pain. The next most important step in the history of the treatment of this disease was the operation of posterior root resection devised by Spiller

rhage, the blood going up as well as down, and then the patient had dark stools afterward. Furthermore, I have seen patients explored for massive hemorrhage and nothing found.

DR TRACY B MALLORY: Do you wish to tell the operative findings, Dr Bartlett?

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persistent edematous anterior cervical lip. The patient was anesthetized and prepared for delivery. Forceps were applied and moderate traction brought the baby's head down on to the perineum. The blades were then removed and the head delivered. There was only a slight tear of the mucous membrane on the left side of the vagina. The placenta was delivered with a great deal of difficulty by the Credé method but finally came away intact. There was considerable bleeding following the birth of the placenta. A hot intrauterine douche was therefore administered followed by alcohol.

The morning following delivery the temperature was 98°F. At 1 p.m. it was 101.2°F. The pulse went to 120. The patient complained of tenderness in both lower quadrants. There was some voluntary spasm in the lower abdomen and slight distention. The patient seemed quite ill. Another intrauterine douche was administered and ice caps were applied to both lower quadrants. Fluids were forced by mouth and she was given 30 cc. of whisky every hour.

During the course of the next three days the temperature and pulse gradually returned to a normal level. On the tenth postpartum day the patient had a chill and the temperature rose to 103.4°F. The cervix was dilated, and some pus was evacuated from the uterus. Intrauterine douches of sterile water and alcohol were given. At this time the patient still complained of lower abdominal tenderness, which was worse on the left.

During the next week the patient ran a spiking temperature up to 105°F. The pulse ranged around 120. On February 12, seventeen days after delivery, she passed a tapeworm. For some unexplained reason her temperature then became normal and she was discharged four days later. A discharge examination revealed a soft non-tender abdomen, moderate rectocele, slight cystocele and a good perineal body; the uterus was retroverted and drawn to the left and there was considerable induration in the left vault.

Comment. This case occurred in 1912 and is typical of the treatment in vogue at that time. The patient was one of a series of septic cases that occurred during a hospital epidemic. Today it is barely possible that the use of pituitrin and intelligent fundal pressure might have done away with the need of the forceps operation. Certainly today the intrauterine douche which was used to control bleeding and the intrauterine douches followed by alcohol which were used during the febrile course of the convalescence would not have been employed. It might be said that this patient got along well in spite of the intrauterine

douche, not because of it, for certainly no greater contraindication could exist than the physical findings described in this case. Low abdominal pain and spasm suggested beyond question the possibility of tubal involvement and the final examination which demonstrated 'considerable induration in the left vault' bears out the assumption that the infection had spread beyond the uterus. Today the treatment would have been entirely conservative. Uterine and blood cultures would have been obtained, chemotherapy would have been instituted if the cultures had so indicated, ice would not have been applied to the abdomen, and the uterus would have been left entirely alone.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning November 13

BAKINGTABLE

Sunday November 19 at 4:00 p.m., at the Cape Cod Hospital Hyannis. Common Problems of Neurology. Indications for lumbar puncture. Instructor: H. Houston Merritt. Donald E. Higgins, *Chairman*.

BRISTOL NORTH

Thursday November 16 at 4:00 p.m., at the Morton Hospital Taunton. Convulsions in Infants and Children—Etiology and Treatment. Instructor: Louis K. Diamond. Lester E. Butler, *Chairman*.

BRISTOL SOUTH (New Bedford Section)

Friday November 17 at 4:00 p.m., at St. Luke's Hospital New Bedford. Head and Spine Injuries. Instructors: Donald Munro, Robert H. Goodwin, *Chairman*.

ESSEX NORTH

Friday November 17 at 4:30 p.m., at the Lawrence General Hospital Lawrence. Indications for Cesarean Section. Instructor: Thomas R. Goethals. John Parr, *Chairman*.

ESSEX SOUTH

Tuesday November 14 at 4:00 p.m., in the Conference Room of the Salem Hospital, Salem. Syphilis in Pregnancy and the Offspring. Instructor: Francis M. Thurmon. J. Robert Shaughnessy, *Chairman*.

MIDDLESEX EAST

Tuesday November 14 at 4:00 p.m., at the Melrose Hospital Melrose. Cardiovascular Disease. Eleven important questions about heart disease and their answers. Instructor: Paul D. White. Walter H. Flanders, *Chairman*.

MIDDLESEX NORTH

Friday November 17 at 4:45 p.m., at St. John's Hospital Lowell. Gonorrhea in the Female. Instructor: Sylvester B. Kelley. William S. Lawler, *Chairman*.

WORCESTER (Milford Section)

Tuesday, November 14, at 8 30 p.m., in the Nurses' Home of the Milford Hospital, Milford
Complications in Obstetrics Illustrated by Case Histories
Instructor M. V. Kappius Joseph Ash
kins, *Chairman*

WORCESTER (Worcester Section)

Friday, November 17, at 8 00 p.m., in the Staff Room of the Worcester City Hospital, Worcester
Pneumonia Instructor Maxwell Finland
George C. Tully, *Chairman*

WORCESTER NORTH

Friday, November 17, at 4 30 p.m., in the Nurses' Home of the Burbank Hospital, Fitchburg
Medical Complications in Pregnancy Instructor
James C. Janney George P. Keaveny, *Chairman*

CORRESPONDENCE

BLUE CROSS BENEFITS

To the Editor Changes in benefits to Blue Cross subscribers were announced on September 1, 1939, and it is important that all members of the medical profession understand how they affect hospitalization of patients. These changes, approved by the board of directors of the Blue Cross and the State Commissioner of Insurance, were necessary to insure future stability and to protect the interests of all participants. The major changes are as follows: x-ray and anesthesia benefits are eliminated; maternity benefits are limited to half the hospital bill; and tonsil and adenoid operations are not included during the first year of membership. After the first year, the family representative is entitled to full benefits in these cases and his dependents to half benefits.

New certificates of membership will be issued to subscribers to become effective for each at the end of his current subscription year. In other words, a certain portion of the membership will be changed to the new certificate each month. Approximately 6000 subscribers were transferred to the new contract in September; another 13,000 will be changed in October, and so on, with those members enrolled during August, 1938, and August, 1939, remaining unchanged until August, 1940. Subscribers are entitled to all benefits under the old contract until they are transferred to the new certificate.

It is deplorable that benefits to the entire membership had to be limited chiefly because of abuses. Our experience has shown that abuses were practiced by subscribers and physicians alike, although they were, in the majority of cases, due to misunderstanding.

During two years of operation (to September 10, 1939), 225,000 subscribers were enrolled and total hospital bills paid in the amount of \$1,225,000 for 25,000 patients, this sum representing about 85 per cent of the earned income for the period. With the Blue Cross's paying hospital bills for 25,000 patients, certainly hundreds of persons have been enabled to pay physicians' fees who otherwise would have received free care.

Specimen copies of the new certificate are available to physicians on request.

R. F. CAHALANE, *Executive Director*,
Associated Hospital Service Corporation.

21 Milk Street,
Boston

NEW ENGLAND PEDIATRIC SOCIETY

To the Editor The attention of the officers of the New England Pediatric Society has been called to the fact it is believed generally that membership in the society is limited to pediatricians. This impression is entirely erroneous. The New England Pediatric Society is an organization devoted to the dissemination of a better understanding of the problems of infancy and childhood; its membership includes many practitioners other than pediatricians. Its purpose can be accomplished only by enlarging the membership to include a greater number of physicians in New England who are interested in the care of infants and children. Any qualified physician who has such an interest is eligible for membership and will be welcomed into the society.

The society has previously held three or four meetings each year, usually in Boston, of clinical and scientific nature. It is planned that additional meetings be held in various parts of New England in order that members unable to attend in Boston can keep informed of progress in this field of medicine. These would consist of round table discussions or clinical demonstrations rather than didactic lectures. Such meetings would necessarily be at the instigation of the local or county medical groups and would be under the direction of some physician provided by the New England Pediatric Society.

Inquiries should be addressed to the secretary.

R. CANNON ELEY, *President*
JAMES M. BATES, *Secretary*

1101 Beacon Street,
Brookline, Massachusetts

NOTICES

REMOVAL

FRED A. SIMMONS, M.D., announces the removal of his office to 264 Beacon Street, Boston.

ANNOUNCEMENT

KENDALL B. CROSSFIELD, M.D., announces the opening of an office at 99 Bay State Road, Boston.

BOSTON DISPENSARY

A luncheon meeting of the clinical staff of the Boston Dispensary will be held on Friday, November 24, in the auditorium of the Joseph H. Pratt Diagnostic Hospital at 12 00 noon. At 12 30 p.m., Dr. Henry A. Chittenden will speak on 'Cardiocasualties.'

An invitation is extended to all who are interested in the luncheon charge to non members is 35c.

JAMES M. BATES, M.D., *Secretary*

BOSTON LYING IN HOSPITAL

Professor Bernhard Zondek will speak on 'Ovulation and Menstruation' at the Boston Lying in Hospital, Friday evening, November 17, at 8 15.

Members of the medical profession are cordially invited to attend.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Dr. Burrill B. Crohn, chief of the Genitoinfectious Service and associate in medicine at Mt. Sinai Hospital, New York City, will speak on 'Regional Ileitis' in the lecture hall of the Joseph H. Pratt Diagnostic Hospital, Saturday, November 18, at 8 15.

morning November 25 at 9-00 Physicians and medical students are cordially invited to attend

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association 554 Columbus Avenue, Boston on Tuesday, November 21, at 12 o'clock noon. Dr. Oscar F. Cox, Jr. will speak on "Gonococcal Infection."

Physicians are cordially invited to attend.

JOHN B. HALL, M.D. *Secretary*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday November 14 in the amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance) at 8:15 p.m. Dr. Soma Weiss will preside.

PROGRAM

Presentation of Cases.

Hemolytic Streptococcal Infections Their importance in acute and chronic diseases. Dr. Chester S. Keefer

Medical students and physicians are cordially invited to attend.

ROBERT M. ZOLLINGER, M.D. *Secretary*

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide, former concertmaster with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra every

Thursday at 8:30 p.m., in Studio A Station WMEA 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430)

CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the Carney Hospital will be held in the Andrew Carney Assembly Room on Monday morning, November 20 at 11:30

PROGRAM

Case Reports.

X-ray Visualization of the Biliary Tract. Dr. Herbert H. Finn. Discussion by Drs. A. McK. Fraser, A. J. Leary, L. F. Curran, J. J. Todd and W. C. Moloney

Physicians and medical students are cordially invited to attend.

ROY J. HEFFERNAN, M.D., *Secretary*

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday November 15 from 2 to 4 p.m. Drs. William C. Quinby and Soma Weiss will speak on Dysuria. A clinicopathological conference, conducted by Dr. Elliott C. Cutler will take place from 4 to 5 p.m.

On Thursday November 16, from 8:30 to 9:30 a.m. there will be at the Peter Bent Brigham Hospital a combined clinic, conducted by Dr. Elliott C. Cutler of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER, M.D. *Secretary*

LAWRENCE CANCER CLINIC

The regular Lawrence Cancer Clinic, to be held at Lawrence General Hospital 1 Garden Street Lawrence, on Tuesday November 21 at 10:00 a.m., will be a demonstration and teaching clinic for physicians, with Channing C. Simmons, M.D., of Boston, present as consultant. Physicians of the north half of Essex County are invited to accompany any of their patients whom they desire to have this service or to send them with a note. A report will be returned to every physician who sends a patient. The service is gratis. Any physician is welcome to attend the clinic.

This clinic is endorsed by the Committee on Postgraduate Instruction of the Massachusetts Medical Society

ROY V. BAKETEL, M.D.,
CHARLES J. BURGES, M.D.,
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HARRY H. NEVILL, M.D.,
THOMAS V. UNTER, M.D.
J. FORREST BURNHAM, M.D., *Chairman*

NEW ENGLAND PATHOLOGICAL SOCIETY

The next meeting of the New England Pathological Society will be held on Thursday evening November 16, at 8:00 at the Peter Bent Brigham Hospital

Dr. Paul R. Cannon professor of pathology at the University of Chicago, will speak on "The Relation of Flocculating Antibodies to Tissue Hypersensitiveness and Localized Disease."

Physicians and students are cordially invited to attend.

BENJAMIN CASTLEMAN, M.D. *Secretary*

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The annual meeting of the New England Obstetrical and Gynecological Society will be held in Boston on Wednesday December 6.

The Carney Hospital, Massachusetts General Hospital and the Lahey Clinic will hold morning clinics, and an afternoon clinic is to be held at the Boston City Hospital.

INTERNATIONAL COLLEGE OF SURGEONS

The officers of the United States Chapter of the International College of Surgeons cordially invite all physicians and surgeons in good standing to their fourth assembly to be held in Venice, Florida February 11-14 1940. There is no registration fee.

For general information please address Dr. Fred H. Albee, Chairman 57 West 57th Street, New York City. For information about the presentation of scientific papers or exhibits, query Dr. Charles H. Arnold, Secretary of the Scientific Assembly Terminal Building Lincoln Nebraska.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING
MONDAY, NOVEMBER 13

MONDAY NOVEMBER 13

- *12 15 p.m.—1 15 p.m. Clinicopathological conference Dr S Burt Wolbach Peter Bent Brigham Hospital amphitheater
- *12:30 p.m. Massachusetts Tuberculosis League Y W C A Boston

TUESDAY NOVEMBER 14

- 9-10 a.m. Cardiovascular Disorders in the Course of Some Acute Infectious Diseases Dr Conrad Wesselhoeft Joseph H Pratt Diagnostic Hospital
- *10 a.m.—12 30 p.m. Boston Dispensary tumor clinic
- *12 15 p.m.—1 15 p.m. X ray conference Dr Merrill C Sosman Peter Bent Brigham Hospital amphitheater
- *8 15 p.m. Harvard Medical Society Amphitheater of the Peter Bent Brigham Hospital

WEDNESDAY NOVEMBER 15

- 9-10 a.m. Hospital case presentation Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital
- *12 m. Clinicopathological conference Children's Hospital amphitheater
- *2 p.m.—4 p.m. Joint medical and surgical clinic Peter Bent Brigham Hospital

THURSDAY NOVEMBER 16

- *8 30 a.m.—9 30 a.m. Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital at the Peter Bent Brigham Hospital
- *9-10 a.m. Recent Advances in Hematology Dr H G Brugsch Joseph H Pratt Diagnostic Hospital

FRIDAY NOVEMBER 17

- *9-10 a.m. Peripheral Vasoconstriction in the Causalgia Like States Dr John Homans Joseph H Pratt Diagnostic Hospital
- *10 a.m.—12 30 p.m. Boston Dispensary tumor clinic
- 12 m. Clinical meeting of the Children's Medical Service Massachusetts General Hospital Ether Dome
- *12 m. Urological conference at the Massachusetts General Hospital lower amphitheater Out Patient Department
- *8 15 p.m. Boston Lying in Hospital Professor Bernhard Zondek will speak on Ovulation and Menstruation

SATURDAY NOVEMBER 18

- *9-10 a.m. Hospital case presentation Dr S J Thannhauser Joseph H Pratt Diagnostic Hospital
- *10 a.m.—12 m. Medical staff rounds of the Peter Bent Brigham Hospital Conducted by Dr Soma Weiss

*Open to the medical profession

NOVEMBER 13—Massachusetts Tuberculosis League. Page 718 issue of November 2

NOVEMBER 14—Harvard Medical Society Page 759

NOVEMBER 15—Peter Bent Brigham Hospital Joint medical and surgical clinic Page 759

NOVEMBER 16—Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital Page 759

NOVEMBER 16—New England Pathological Society Page 759

NOVEMBER 17—Boston Lying in Hospital Page 758

NOVEMBER 20—Carney Hospital Monthly clinical meeting and luncheon Page 759

NOVEMBER 21—South End Medical Club Page 759

NOVEMBER 21—Lawrence Cancer Clinic Page 759

NOVEMBER 24—Boston Dispensary Luncheon meeting of the clinical staff Page 758

NOVEMBER 25—Joseph H Pratt Diagnostic Hospital Page 758

DECEMBER 2—American Board of Obstetrics and Gynecology Page 1019 issue of June 15

DECEMBER 6—New England Obstetrical and Gynecological Society Page 759

DECEMBER 8—William Harvey Society Page 676 issue of October 26

DECEMBER 14—Pentucket Association of Physicians. 8 30 p.m. Hotel Bartlett Haverhill

JANUARY 6 JUNE 8-11 1940—American Board of Obstetrics and Gynecology Page 160 issue of July 27

JANUARY 22-25 1940—American Academy of Orthopaedic Surgeons Hotel Statler Boston

FEBRUARY 11-14—International College of Surgeons Page 759

MARCH 2 JUNE 8 and 10—American Board of Ophthalmology Page 719 issue of November 2

MARCH 7-9 1940—The New England Hospital Association Hotel Statler Boston

MAY 14 1940—Pharmacopoeial Convention Page 694 issue of May 25

JUNE 7-9 1940—American Board of Obstetrics and Gynecology Page 1019 issue of June 15

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH

NOVEMBER 15—Heart Disease in Pregnancy Dr C Sidney Burwell Beverly Hospital Beverly

DECEMBER 6—'Pyelonephritis and Its Relation to Other Inflammatory Diseases of the Kidney' Dr Soma Weiss Salem Hospital Salem

JANUARY 3 1940—Head Injuries Dr John S Hodgson Danvers State Hospital Haverhill

FEBRUARY 14—Cough Sputum Hemoptysis—How shall they be investigated? Dr Reeve H Betts Essex Sanatorium Middleton

MARCH 6—'Experimental' and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections Dr Champ Lyon Lynn Hospital Lynn

APRIL 3—Addison Gilbert Hospital, Gloucester

MAY 8—Annual meeting Salem Country Club Peabody

HAMPSHIRE

JANUARY 10 1940

MARCH 13

MAY 8

All meetings are held at 11 30 a.m. at the Cooley Dickinson Hospital Northampton

MIDDLESEX EAST

NOVEMBER 15

JANUARY 10 1940

MARCH 20

MAY 15

Meetings are held at 12:15 p.m. at the Unicorn Country Club Stoneham.

PLYMOUTH

NOVEMBER 16—Moore Hospital Brockton

JANUARY 18 1940—Brockton Hospital Brockton

MARCH 21—Goddard Hospital Brockton

APRIL 18—State Farm

MAY 16—Lakeville Sanatorium Lakeville

SUFFOLK

NOVEMBER 29—Scientific meeting Treatment of Syphilis Dr Harold T Hyman, Dr Louis Chargin and Dr William Lelfer of New York City

JANUARY 31 1940—Scientific meeting Subject to be announced later

MARCH 27—Scientific meeting Symposium on Ulcerative Colitis and Diarrhea Under the direction of Dr Chester M Jones

APRIL 24—Annual meeting in conjunction with the Boston Medical Library Election of officers Program and speakers to be announced later

BOOKS RECEIVED FOR REVIEW

Atlas of Surgical Operations Elliott C Cutler and Robert Zollinger 181 pp New York The Macmillan Co, 1939 \$8 00

A Topographic Atlas for X-Ray Therapy Ira I Kaplan and Sidney Rubinfeld 120 pp Chicago The Year Book Publishers, Inc., 1939 \$4 00

An Introduction to Medical Mycology George M. Lewis and Mary E. Hopper 315 pp Chicago The Year Book Publishers, Inc., 1939 \$5 50

Problems in Prison Psychiatry J G Wilson and M. J. Pescor 275 pp Caldwell, Idaho The Caxton Printers, Ltd., 1939 \$3 00

You and Heredity Amram Scheinfeld Assisted by Morton D Schweitzer 434 pp New York Frederick A Stokes Co, 1939 \$3 00

Gynecology Medical and surgical P Brooke Bland. Assisted by Arthur First. Third edition 843 pp Philadelphia F A Davis Co, 1939 \$8 00

Diagnostic Signs, Reflexes and Syndromes W Egbert Robertson and Harold F Robertson 309 pp Philadelphia F A Davis Co, 1939 \$3 50

A Text-Book of Occupational Diseases of the Skin Louis Schwartz and Louis Tulipan. 799 pp Philadelphia Lea & Febiger, 1939 \$10 00

Physiology in Health and Disease Carl J Wiggers. Third edition 1144 pp Philadelphia Lea & Febiger, 1939 \$9 50

The New England Journal of Medicine

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VOLUME 221

NOVEMBER 16, 1939

NUMBER 20

MASSACHUSETTS MEDICAL SOCIETY

Section of Dermatology*

THE WAR AGAINST SYPHILIS

E. LAWRENCE OLIVER, M.D.†

BOSTON

THE history of syphilis is the most dramatic story in the history of disease, and its control is one of the most important sanitary problems in medicine. The portion of this paper concerning the history of syphilis is based largely on that admirable book, *The History and Epidemiology of Syphilis* by William A. Pusey,¹ which was published in 1933.

Syphilis appeared in Europe with explosive suddenness at the end of the fifteenth century. In 1494, Charles VIII of France sent his troops into Italy with the object of capturing Naples, which object was attained February 22, 1495. During the next few months, a new disease broke out with such violence among his troops that before the spring of 1495 was over his army was forced to abandon the city and retreat in confusion. These troops, scattering over Europe, sowed the seeds of the disease wherever they went, so that within the short space of two years the malady had spread with astounding rapidity over most of Europe, including the British Isles. The fight against syphilis began at that time. Bloch states that in 1496 the Parliament of Paris decreed that all persons infected with the disease should leave the city within twenty-four hours. The next year the Privy Council of Scotland passed a law ordering banishment to the island of Inchkeith for all the inhabitants of Edinburgh who were victims of the disease.

At this time the new disease had no exact name; the Italians called it the French disease, the French called it the Italian disease, the Russians called it the Polish disease. However, all believed it

was a new disease which had not previously been encountered in Europe. Whence did it come? There is much to indicate that the disease came from the New World, having been brought to Europe by the sailors of Columbus. No description of the syphilitic syndrome has been found prior to 1493. The first Spaniards who recognized syphilis called it the disease of Española, which signified the disease of Haiti. Another very potent reason for believing that syphilis was a disease new to Europe was its malignancy during the first fifty years after its explosive outbreak. The high fever, the intense pains in the joints, the severity of the rash, the even frequent death in the secondary stage, all point to a disease to which Europeans had acquired no natural immunity.

For written evidence that syphilis came from the New World we have the work, printed about 1515 of Diaz de Isla, who was a practicing physician in Barcelona in 1493. He states that syphilis was unknown in Europe before 1493, that its home was in Haiti, and that he himself had treated several of Columbus's sailors soon after their arrival in Barcelona in 1493.

From Europe the disease spread to Africa and the Orient. The researches of Okamura and Suzuki for Japan and China and those of Jolly for India indicate that syphilis appeared in those countries only after contact with Europe. In India the disease was recognized in 1498 after the arrival of Vasco de Gama, who had left Portugal in 1497.

Mercury was employed as a remedy very early in the history of syphilis. This is not surprising as mercury had been used for a long time by Arabian physicians in leprosy and psoriasis. Paracelsus is given credit for its first use in the treatment of syphilis.

*This section meeting was held, and the following three papers read during the annual meeting of the Massachusetts Medical Society, Worcester, Massachusetts, June 6, 1939.

†Clinical professor of dermatology and syphilology emeritus, Harvard Medical School, member of Board of Consultants, Massachusetts General Hospital, Boston.

In the seventeenth and early eighteenth centuries most if not all the lesions of syphilis had been gumma, syphilitic meningitis and lesions of the bones, spleen and kidneys. Lancelotti before 1720 had noted a relation between diseases of the heart and blood vessels, including aneurysm, to syphilis. Before the end of the eighteenth century hereditary syphilis was well known. Extragenital chancres were recognized, and the dangers of contagion by kissing or from contaminated drinking cups were emphasized.

Wallace, of Dublin, in 1834 was the first to introduce potassium iodide in the treatment of syphilis.

In 1905 Schaudinn and Hoffmann discovered the *Treponema pallidum*, and in 1906 Wassermann and others demonstrated the value of serum tests in the diagnosis of syphilis. Three years later Ehrlich began the use of arsphenamine in treatment. At first it was believed that one treatment with arsphenamine would cure the disease. Though this theory soon was shown to be fallacious, nevertheless arsphenamine has remained the most valuable drug in the treatment of the disease.

The value of personal prophylaxis by the use of 33 per cent calomel ointment within a few hours after exposure was demonstrated by Metchnikoff² in 1906. The results of this method of prophylaxis in the United States Army during the World War were amazing. It is unfortunate that this method is not better known. As Pusey says

Any method of this sort has been regarded by a part of the community as immoral and an encouragement to sexual license. If syphilis is to be regarded as a proper punishment for sexual irregularity, then all attempts to prevent its spread are unjustifiable and the whole effort against it falls to the ground. But it is hard to believe that intelligent men and women that pretend to be humane will, as a class, accept this attitude.

It is probable that no other measure for the control of syphilis would be as valuable as the wide diffusion of knowledge as to the extraordinary value of 33 per cent calomel ointment, if used within five hours after exposure.

In regard to laws designed to control syphilis, the Swedish Act³ of 1918 has proved so successful that it has drawn the attention of the entire world. During the sixteen years following the passage of this act, the number of cases of early syphilis in Sweden fell from the rate of 10 in every 10,000 population to less than 1.

The principal features of this act have been summarized as follows. Every person suffering from venereal disease must submit to medical treatment and follow instructions. Such treatment can be furnished only by a qualified prac-

titioner. Free treatment is provided for those who need it. All cases not previously treated by another physician must be forthwith reported to the local inspector of health, but without divulging the patient's name. The name is to be entered on the physician's record but is not reported to the authorities unless the patient defaults in treatment or unless for some other reason coercive measures are called for. The obligation rests on the physician to ascertain the source of infection if possible and to convey the name and address of such alleged source, when obtainable, to the local inspector of health, who then takes steps to have the person examined.

In Norway there is no free treatment of syphilis except for sailors and indigents.³ The government has considered adopting the Swedish law, but the expense of carrying out the provisions of such a law has so far prevented its adoption.

In Holland there is no notification of cases and no compulsion to undergo treatment, but since 1925 much valuable work has been done by social workers, health visitors and nurses, who endeavor to see that patients are properly treated and followed up.³

In England efforts to control syphilis go back to 1875, but it is only since 1914 that free treatment has been available to every syphilitic patient regardless of financial status.³ In 1935 there were 185 treatment centers in England and Wales and 52 in Scotland. Patients may be urged to continue treatment, but there is no compulsion. They may discontinue treatment at any time, the British principle being that personal liberty and freedom of action must be respected. Education of the public in regard to venereal diseases by wide advertising of the venereal clinics is an important factor in the British plan.

Although figures indicate a considerable decrease of early syphilis in England—a 34 per cent drop from 1931 to 1935—it is believed by some that these figures are misleading, as an ever increasing number of syphilitic patients treated by private physicians do not appear in the official records.

The extraordinarily successful results of the law in Sweden are probably due to the fact that the Swedish public has a marked respect for the law and the medical profession. It is certain that respect for the law is not one of the American virtues. We all know how little respect was paid to the Prohibition Amendment.

For some years many of our states, Massachusetts among them, have had laws more or less similar to those of Sweden, providing that all cases of syphilis shall be reported to the health authori-

ties, but without names or addresses. If patients stop treatment against advice they become reportable by name and address.

Successful results from such laws naturally depend on its administration and on the co-operation of physicians. Since the passage of this law in Massachusetts, statistics indicate a marked decrease in the incidence of early syphilis, with an increase in the number of late cases that would naturally be expected with the wider use of rum tests.

Since Surgeon General Thomas Parran in 1936 started his campaign to bring the problem of syphilis control to public attention the American public is demanding laws designed to safeguard marriage and the unborn child.

In the *Journal of Syphilis, Gonorrhea and Venereal Diseases* for May, 1939 there is a summary of a debate on the value of such premarital examination laws, Dr. William Snow upholding them and Dr. N. A. Nelson, director of the Division of Genitoinfectious Diseases, Massachusetts Department of Public Health opposing them. Now's arguments are as follows:

The laws constitute a valuable method of case finding. It is first essential in any program for the control of syphilis.

They will decrease the transmission of syphilis in marriage.

They will decrease the incidence of congenital syphilis.

By insistence on blood tests by approved laboratories they will raise the standard of laboratory performance throughout the country.

They will have a general educational value in keeping the problem of syphilis closely in the public mind.

Nelson's arguments are these:

In the diagnosis of syphilis emphasis is laid almost wholly on the laboratory.

The specificity of serological tests for syphilis in the best of hands is technically short of perfect. False positives in supposedly good laboratories have been estimated at times as high as 10 per cent.

In two reasonably prevalent diseases in this country (malaria and infectious mononucleosis) biological false positive results occur in a significant proportion of cases, and far too little positive modern information is available as to biological false-positive tests in many other conditions. Moreover evidence is accumulating which suggests that the blood of a small but as yet unknown proportion of perfectly normal persons may from time to time, or permanently contain enough reagin or reagin-like substance to cause a transitory or permanent biological false positive serological test. Therefore, a considerable number of non-syphilitic persons will be caused undue harm, delay in marriage and expense due to the unraveling of the significance of false positive or doubtful results. The case reports of Stokes and Ingraham¹ make clear that this is already happening.

The blood test is a wholly invalid indicator of infectiousness or non-infectiousness in syphilis.

The law will not serve its purpose in preventing the spread of syphilis within marriage. Premarital intercourse

is already so frequent as to make the law an effort to lock the stable door after the horse has been stolen. In the social and economic groups having the highest incidence of syphilis the incidence of common-law marriages and illegitimacy will be increased.

Regardless of arguments for or against premarital examination for syphilis, it is evident that laws of this kind will soon be passed in most of our states. It would seem, then, to be the part of wisdom for our medical societies to take a larger part in this type of legislation, and to approve such laws as leave the decision as to infectiousness in the hands of the physician, where it belongs for it is the physician who will see and examine those desiring marriage. It is the physician who is best able to evaluate the result of the blood test and best qualified to give advice on the question of marriage if the test is reported positive. The Committee on State and National Legislation of the Massachusetts Medical Society has recently gone on record as approving such a law for our state.²

There are now premarital examination laws in twenty-six states of the Union. In three states (Illinois, Michigan and Kentucky) marriage is forbidden to all persons showing positive serological tests.³ It would seem that the passing of such laws must be due to a combination of ignorance and mass hysteria. It is conceded by syphilologists the world over that a positive test is no criterion of infectiousness. If human rights are to be totally disregarded and if this hysteria keeps growing at the present rate it would be hardly surprising if a law were suggested demanding universal blood tests, with euthanasia for all those with positive reactions. Such a law would prove effective but, to say the least, would be a bit unfair.

Five states now have laws requiring the reporting of the names of all patients with syphilis. It is probable that such laws will prove worse than useless. Patients with venereal diseases desire secrecy above all, reporting them by numbers does not disturb them but they do not like the idea of having their names placed on the files of public authorities. Such laws encourage timid patients to attempt self-treatment or to go without any treatment thus prolonging the period of their infectiousness. Of course their names are supposed to be kept in inviolate secrecy but state secrets have been known to leak out in the past. Even blackmail would seem to be a possibility if the names should come to the attention of an unscrupulous individual employed by a department of health. Strictures of the disease in states with such laws are apt to be worthless, for many physicians, believing in the sanctity of privileged communications, will not obey such laws.

As regards the relation of syphilis to pregnancy, New York in 1938 was the first state to pass a law requiring that blood tests be made on all pregnant women. Several years ago an investigation⁷ had shown that although the public clinics in New York were doing blood tests on all pregnant women, only about half the physicians attending private obstetric cases were testing their patients.

Treatment of pregnant women with syphilis is notably successful in preventing congenital syphilis, provided the patient is seen before the fifth month of pregnancy. In many maternity hospitals the incidence of congenital syphilis has been greatly reduced since blood testing has been the rule. If a considerable number of cases of congenital syphilis can be prevented by such laws, there is little reason to object to them for any cause other than the expense of administration.

In the war against syphilis, the public should be made to realize the wide prevalence of the disease. It should be taught that there are efficient means of prevention, that there are efficient methods of diagnosis and treatment, that the earlier a case comes under treatment the greater the probability of a cure, without minimizing the fact that treatment is of great value in all stages of the disease. It should also be shown that hereditary syphilis may be practically abolished if women with the disease are placed under efficient treat-

ment before the fourth or fifth month of their pregnancy.

If it be conceded that the control of syphilis is one of the most important problems in medicine, it is evident that considerably more time should be allotted for instruction concerning syphilis in our medical schools.

If the public can be taught the value of prophylaxis, as well as the importance of early diagnosis and treatment, if the medical profession as a whole is made to realize the importance of sufficient treatment, especially in the early stages of the disease, and if the fight is not hampered by ill-advised and unenforceable legislation, it is hoped and believed that rapid progress will soon be evident in the war against syphilis.

20 Fairfield Street.

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- 1 Pusey, W. A. *The History and Epidemiology of Syphilis: The Gorman Lectures University of Illinois 1933*. 113 pp. Springfield, Illinois and Baltimore. Charles C Thomas 1933.
- 2 Metchnikoff, E. *Sur la prophylaxie de la syphilis*. Ann Inst Pasteur 21:753-759 1907.
- 3 Report of the New York City commission to investigate the prevalence and control of syphilis and gonorrhea in Scandinavian countries and in Great Britain. Am J Syph Gonorr & Ven Dis 20:7-63 (Supp. July) 1936.
- 4 Stokes, J. H. and Ingraham, N. R. Jr. Syphilis and the law with discussion of false positive blood serologic test. J A M A 112:1113-1143 1939.
- 5 Lund, C. C. Control of syphilis. New Eng J Med 220:648 1939.
- 6 Nelson, N. A. personal communication.
- 7 Exner, M. J. Syphilis in pregnancy: report of a study. J A M A 106:488-490 1936.

LUES LATENS*

PAUL A. O'LEARY, MD†

ROCHESTER, MINNESOTA

A FEW moments' reflection will bring to light the fact that the bulk of our knowledge of syphilis has been acquired during the last twenty-five years. Although the debate continues as to whether Columbus imported the disease to Europe on the return from his second trip to this country or whether it had existed on the Continent before his time, the information gathered during the last few years has materially changed our conception of a disease that has been prevalent for more than four hundred years. During the quarter of a century that has gone we learned of the limitations of the drugs which were originally thought to be, or at least were hoped to be, panaceas for a disease which requires from fifteen to twenty years

to develop its serious sequelae. If the physician who became interested in syphilis when the arsenophenamines were first introduced has recently had either the opportunity or the incentive to survey the patients who were well treated twenty years ago, he will find that, although some of them may still react positively to a blood test, very few manifest any of the late complications of the disease. A terse statement of the accomplishment of the modern treatment of syphilis, as a result of surveys by the Co-operative Clinic Group,¹⁻⁴ may be briefly summarized as follows: although intensive specific treatment of early syphilis does not cure all patients, it does prevent the development of the late complications of the disease in all but 2 per cent of the patients treated. It is obvious, then, that although our efforts are still directed toward cure, and whereas this is accom-

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plished in approximately 85 per cent of the cases, the fact that it is possible to prevent the appearance of the incapacitating and death-dealing complications in 98 per cent of the patients is the basis for the present state of enthusiasm for the intensive treatment of early syphilis. For many years the thought of cure was limited to cases in which treatment was started during the early phases of the disease, but we now recognize that cure is also possible when the patient begins treatment after the disease has been present for some years. Likewise, it is now established that spontaneous cure occurs in approximately a third of the cases in which the disease is acquired.⁷ Such cures occur in cases in which patients do not receive any treatment whatsoever for syphilis. Since the period of observation following malarial therapy in many cases is now more than fifteen years there is substantial evidence at hand that cures also occur after this type of treatment in cases with types of neurosyphilis which were unresponsive to any therapeutic program previous to the fever-therapy era. The basis for this statement is the result of the pathological studies of the brains of patients with general paresis who were treated with malarial therapy ten or more years ago.

The means of estimating cure in a case of syphilis are based on clinical observation for at least five years after the patient has become clinically and serologically negative.⁸ Serologic negativity applies to both blood and spinal fluid tests. With each year after the expiration of the five year period that the patient continues to remain clinically and serologically negative, the likelihood of cure becomes greater.

Before discussing latent syphilis or latency a brief résumé of the present-day conception of the course of the disease would seem advisable. For the expressions "first," "second" and "third" stages have been substituted early⁹ or acute, "latent" and "late" syphilis. The reason for adopting these terms is the more thorough understanding of the biological course of the disease. The period of early or acute syphilis includes the first two years of the period in which the patient is infectious and during which the majority of the relapses of all types occur. Unfortunately it cannot be said that all patients cease to be infectious at the end of the second year, because one occasionally encounters individuals who maintain infectious lesions for many years. However, such cases are not common and are becoming rare.

Latent syphilis follows early syphilis, and is characterized by the absence of clinical signs and symptoms of the disease. The real significance

of the period of latency depends on whether it remains as a permanent state or is only temporary.⁹ In those cases in which latency is temporary, late syphilis may appear in the form of cardiovascular disease, neurosyphilis, osseous or cutaneous lesions or any of the other numerous late manifestations.

Latency may be defined as that period of the disease, after the disappearance of the signs of acute syphilis, when the patient is free of both signs and symptoms. Latency has been subdivided into early and late types. Early latency includes the third and fourth years, while late latency embodies the period beyond the fourth year in which the patient remains free of clinical evidence of the disease. The significance of early and late latency will be elaborated on subsequently.

Latency has been further classified by Moore and others⁷ into clinical, serologic and pathologic types. Clinical latency is that phase characterized by a complete absence of clinical signs or symptoms of syphilis. Serologic latency implies that although the results of serological tests are negative there are still foci of active syphilitic disease in the patient. Pathologic latency denotes an asymptomatic phase of the disease in which, however, nests of *Treponema pallidum* have become walled off in one or more of the viscera, but no pathologic reaction has developed in situ as a result.

Of the types encountered by physicians, clinical latency is the most frequent and its importance overshadows the other types from the clinician's and patient's viewpoints because it offers a variety of problems in its management. In reality, however, the pathologic type of latency is more important, because the subsequent course of the disease is dependent on the activity of the biologic processes. Many of the patients who acquire syphilis have a chancre, followed by lesions on the skin and mucous membranes. By no means do all these patients have an obvious chancre and the subsequent cutaneous manifestations of the disease and many of them pass through the early phase of syphilis without displaying clinically recognizable manifestations of these commonly anticipated signs. Perhaps the chancre may be so small as to pass unnoticed or the cutaneous symptoms so mild that they are not recognizable. Following the involution of the early signs of the disease, either as the result of treatment or spontaneously the patient then passes into the period of early latency. His defense mechanism if it is active has by this time started to function, with the result that he does not display further evidence of the disease. Within a period of another two years he passes into the phase of late latency. If during the early stage of the infection the individual's defense mechanism is lacking, either from inherent

qualities, inadequate treatment or virulency of the organism, he does not slip through the early period so asymptotically. He may have lesions on the skin or the mucous membranes which continue to be a source of infection to others, or he may manifest evidence of recurrence of the disease in the central nervous system, viscera or one of the organs of special sense. These recurrences may show a rapid response to treatment, or they may be the forerunners of a serious course of events which result in the patient's incapacity or death.

Comment has been made that latency which is only of a temporary nature is a serious form of syphilis, for the following reasons. The acute signs subside either spontaneously or as a result of treatment, and the patient passes into the early phase of latency. He is asymptomatic, and hence feels well and either forgets or minimizes the fact that he has syphilis, however, during the period of the acute syphilis, invasion of the central nervous system or the viscera by the *Treponema pallidum* has occurred. A pathologic reaction takes place at these sites, and some ten or more years later the patient presents clinical signs that the organ has become definitely involved by the syphilitic process. In other words, although the patient has been without symptoms of the disease during this ten-year period, the infection has been present in an asymptomatic form and all the while amenable to treatment. This serves to emphasize one point in particular, namely, that the invasion of the various systems takes place at the time of the dissemination of the spirochetes during acute syphilis, although the clinical evidence of involvement may not become obvious for several decades. Thus it is understandable that the term "temporary latency" is synonymous with asymptomatic syphilis. In contrast with the course of events just described is the case which passes through the early phases of the disease to a state of latency that remains permanent. Such patients never manifest signs of syphilis of the central nervous system, viscera or other organs but continue to remain asymptomatic during the remainder of their lives. The patients who are fortunate enough to maintain this state may do so as the result of treatment or spontaneously, perhaps as the result of an efficient defense mechanism against the disease. The fact that a permanent state of latency develops in some cases does not mean that invasion of one or the other of the various systems did not occur. It does mean, however, that even though such invasion took place the spirochetes were walled off or destroyed in situ so that a pathologic reaction at that point did not develop. The observation of a large group of patients with early syphilis and invasion of the

central nervous system as evidenced by a positive reaction of the spinal fluid has revealed that many of them will overcome this invasion, that the reaction of the spinal fluid will become negative and that signs of neurosyphilis will subsequently not be demonstrable.

Hence, it may be said that a patient who is not cured of the disease during the acute phase does well to obtain a permanent state of latency. It may also be said that permanent latency, from the patient's viewpoint, is equivalent to cure.

Serologic latency implies that although the results of serological tests are negative the patient still has active foci of syphilis. This was a common finding in the period of the old serological technique but now with the newer flocculation procedure the incidence of serologic latency is becoming less. With the development of more sensitive tests which the future will no doubt bring, the patient with serologic latency will become rare.

Pathologic latency means that active *Treponema pallidum* are present in tissue but that a pathologic reaction on the part of the host to the invader, the form of minute or massive gummas, is lacking. Warthin fostered this conception of latency and by so doing has prevented enthusiastic syphilologists from speaking too glibly of the incidence of cure in a group of patients treated as observed clinically. Warthin's conception of pathologic latency is still a subject for debate and proof is dependent on the findings at necropsy.

The diagnosis of latency is based on the following: the history and the approximate date at which the infection was acquired, a negative reaction of the spinal fluid, absence of clinical signs or symptoms of syphilis, especially in the central nervous or cardiovascular system, some knowledge of the type and amount of treatment previously given, a negative or positive result of a flocculation test on the blood, and the opportunity for frequent clinical re-examinations.

It is of value to know the duration of the disease in appraising the state of latency, hence, some information as to the date on which the acute signs of the disease were recognized is essential. Unfortunately, these data are obtainable in only about half the cases, therefore the historical information starts from the time that a positive result with a serological test was obtained. The advantage of having definite knowledge in regard to the duration of the disease permits one to classify the patient in either the early or late phase of latency. Early latency is of less significance than late latency because the former is of short duration, while the latter becomes greater each year that the patient retains latency as a permanent state. An individual who has had syphilis for twenty-five years and is found to be asymptomatic

will in all probability remain so. The same, of course, cannot be said of the patient in whom the disease has been present only four years.

A negative reaction of the spinal fluid is essential for a diagnosis of latency. If this is found in a case in which syphilis has been present for more than five years, the patient can be assured to the extent of 99 per cent that the spinal fluid will always remain negative, however if the disease has been present for less than five years this assertion cannot be made until sufficient time has elapsed and a subsequent examination of the spinal fluid at the end of the course of treatment has been made and has given a negative result. In a case in which the reaction of the spinal fluid was positive at the time of the acute syphilis, repeated examinations of the fluid are necessary for a period of five years, especially if the results of tests on the blood remain positive or if a change from negative to positive occurs.

The diagnosis of latency cannot be made if the patient displays any signs or symptoms of syphilis. Likewise, in some cases, especially those in which historical data are lacking, such a diagnosis can not be made at the time of the first clinical examination even though such examination does not disclose any manifestations of syphilis. As the disease is prone to involve almost any of the organs of the body a complete clinical survey is essential, although special scrutiny should be directed to the cardiovascular system. A roentgenographic examination of the heart and aorta is essential and even though the report is negative the roentgenogram should be kept as a part of the patient's record for future comparison. In addition careful examination of the pupils, the deep tendon reflexes, the mucous membranes, the liver, the hearing and the osseous system should be made not only at the original examination but also at each subsequent examination of the patient. It is only by such re-examination that it is possible to demonstrate that the patient has the permanent state of latency.

Some knowledge as to the type and amount of treatment previously received is also of aid in recognizing the state of latency. Although this information is of special value in determining the subsequent course of treatment to be followed it is also a guide to the status of the patient's defense mechanism. The individual who has received more than the average amount of treatment usually given in cases of acute syphilis—thirty injections of arsphenamine and sixty injections of bismuth—and still manifests evidence of syphilis is lacking in his forces of resistance, whereas the individual who has received only four or five injections of arsphenamine and a few injections of bismuth and shows no signs of infec-

tion probably has an active defense mechanism. For these reasons some information about previous treatment is of value.

Little has been said thus far about blood tests. The reason for this is that the diagnosis or the treatment of latency is not dependent on the status of the reports of flocculation tests on the blood. In many cases in which the disease is in the permanent state of latency, the results of blood tests are persistently positive but the patients never have any manifestations of late syphilis. In a small percentage of cases of active visceral syphilis the results of tests on the blood are negative. Accordingly the results of flocculation or complement fixation tests on the blood are not a significant guide in determining the status of a patient with the latent type of syphilis. The significance of a change in the results of blood tests from positive to negative in a case of latent syphilis in which the patient has been under observation for several years grows in proportion to the number of years the results of the tests remain negative. When the opposite occurs, that is when the result of a test has been negative for some years but becomes positive, a painstaking clinical re-examination should be made in an effort to find the place in which syphilis has become active. If the syphilis has been present for five years or less, the spinal fluid should be re-examined.

Frequent re-examinations of the patient with latency are essential to adequate care and supervision. For the first two years after treatment is stopped these clinical surveys should be made at intervals of six months, and thereafter should be made annually until the disease has been present approximately twenty years. This period is selected because it is known that the majority of the serious complications of the disease are recognizable by the fifteenth year after the infection has been acquired.

The treatment of latency cannot be systematized as can the treatment of early syphilis. The individualization of the therapeutic program in each case is necessarily based on such factors as the sex and age of the patient, the duration of the syphilis, the amount and type of previous treatment and the patient's attitude toward the disease.

If the disease has been present for thirty or forty years, if the patient is sixty years or older if the disease is asymptomatic and if a positive result of a flocculation test is the only evidence that the patient has syphilis, treatment is not warranted. Such a patient is not infectious and has long since passed the period at which complications are likely to develop. One should minimize or ignore the positive results of the blood test in such a case.

If the patient is a young woman who has had the disease for five or six years and has been in

tensively treated during early phases of the disease, and if the result of a flocculation test on the blood is still positive, the administration of two courses of bismuth a year, twenty injections to the course, should be given for at least three and preferably for the next five years. If, however, the young woman has not been treated during the acute phase of the disease she should receive intensive therapy with arsphenamine and bismuth, at least the minimum course of thirty injections of arsphenamine and sixty injections of bismuth should be given by either the continuous or the intermittent method of treatment. Latent syphilis in a woman in the child-bearing period of life requires entirely different treatment than does latency in the male. If such a woman becomes pregnant she must be treated intensively throughout the pregnancy, because in approximately 20 per cent of the women with latency the pregnancy is interrupted by the disease or the child is subsequently found to have syphilis.

Between the examples cited of the patient who is sixty years of age and the young woman are the great bulk of patients who have latent syphilis and who seek negative serological tests and the assurance that they will have no future trouble from the infection. A retrospective clinical study of a large group of these patients showed that, when observed untreated for a period of ten years, 85 per cent of the patients with permanent latency became serologically negative. The same study also demonstrated that serologic reversals appeared about the fifth year when the treatment was limited to bismuth alone. This was about half the time required when arsphenamine and a heavy metal were employed. Accordingly, in a case in which a patient acquired syphilis fifteen years previously and received only a few injections of arsphenamine at that time, a series of twenty injections of bismuth given twice a year for three years may be ample. If, however, there is a suspicion that the latency is of the temporary type, the therapeutic program should consist of the intensive use of arsphenamine and bismuth for at least the so-called minimal course. The factors already mentioned, namely the sex and age of the patient and the duration of the syphilis, rather than the results of serological tests, are a guide as to the

amount of treatment to be administered. In the patient insistent that treatment should be continued as long as the results of blood tests remain positive, the semiannual course of bismuth will probably reverse the results of the tests sooner than will a combined course of arsphenamine and bismuth, and with decidedly fewer complications from treatment.

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DISCUSSION

DR. FRANCIS M. THURMON, Boston. In our experience in the clinics in Metropolitan Boston the cases of latent syphilis comprise approximately 60 per cent of all syphilitic cases with which we have to deal, therefore such cases constitute a very significant problem.

Insofar as the minimum amount of treatment is concerned in the early cases and their follow-up, I am in accord with using the fourth year as a dividing line, because it is usually within the first four or five years of acquired syphilis that the patient is most likely to have a serious relapse or recurrence. As Dr O'Leary has said studies of the heart and aorta are most important, in order to gain some idea as to the condition of the cardiovascular system. I re-emphasize his statement as to the status of the blood test for syphilis, that is, the sole purpose of the test is to detect syphilis. I also concur with Dr O'Leary's statement regarding treatment and prognosis. Emphasis must be placed on the age of the patient, the duration of the disease, and whether or not inroads of syphilis have occurred. Individual consideration is necessary for each case.

I am in complete accord with Dr O'Leary as to Wassermann fastness. A possible consideration is whether the term might not mean a positive serological reaction in the presence of clinical evidence of syphilis. To my mind, the presence of tertiary manifestations, as Dr O'Leary has said, is of great significance, whereas the serological test is not the problem under discussion.

THE INDICATIONS AND CONTRA INDICATIONS OF ROENTGEN RAY THERAPY IN DERMATOLOGY

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THE reasons for the use of radiation in skin diseases require a careful review from time to time in the light of the increased knowledge of the effect of such treatment on cells and their functions, and a re-examination of the arguments against radiation is periodically needed in view of the accumulated experience of many observers. In discussing the subject it is assumed, first, that the apparatus and technic to be used have been accurately standardized, second, that everything has been done to assure a correct diagnosis in each case, and third, that an accurate estimate has been made of those factors in the individual which influence the dosage, such as age, site, coloration and previous treatment.

X rays are almost indispensable in dermatology but should be employed with discriminating judgment and in such a way that no harm will be produced. As with any new method of treatment, x rays have been used too much. Progress in knowledge has advanced, and radiation therapy has approached closer to its proper place in the therapeutic field. Physicians have become more conservative as greater experience has been acquired and as newer methods have developed for the treatment of various dermatoses. It is not only poor technic but a reflection on those who practice dermatology to relieve an acne or an eczema, or cure an angioma or keloid, and years later to be confronted with a consequent atrophy, telangiectasis, pigmentation, keratosis or, in a certain number of cases, carcinoma. Many experienced dermatologists reply that radiation should be used only in conditions which it is impossible to relieve or cure in any other way. The employment of x rays as an agent of treatment in skin disease carries with it the implication that the user has a thorough knowledge of his apparatus and its proper use. It further implies that he is entirely familiar with cutaneous diseases and the dosage required for a particular disease and case and above all knows when to stop. Treatment should always be discontinued when a disease fails to yield to a reasonable amount of treatment.

INDICATIONS

For many years the indications for radiotherapy were based on the experience of various authors as

published from time to time. As time went by, the knowledge of the action of x-rays and radium on cell function was enlarged, and it became possible to base the indications for treatment more and more on fundamental structural effects accomplished by radiation. There are still numerous cases in which the indications are founded on symptomatic factors and other cases in which physiological indications exist do not respond to exposure to x ray or radium. It is impossible to attribute all the accomplishments of such therapy to the physiologic action of rays produced by radium or the x ray tube. I shall, however, attempt to discuss the reasons for treatment, basing them, so far as possible, on the functional changes produced by such rays.

In the first place, there are numerous diseases in which x rays are indicated because of the fact that they inhibit cell function. Most authorities agree that there is no stimulating effect from these rays and that the effect is always adverse. Small doses simply decrease cell function, this decrease being roughly proportional to the amount of radiation given. After a certain point however, large doses begin to produce complete inhibition and ultimate destruction. It is well known that there is much variation in the sensitiveness to radiation of various cells throughout the body. In general it may be stated that young cells, physiologically active cells and cells of the lymphoid series are most easily inhibited. Thereafter in order of radio-sensitivity come epithelial cells, endothelial cells and those of connective tissue, muscle, bone and nerve. This inhibitory effect may be discussed with reference first to glandular activity, second to other tissues and third to hair.

In the group of physiologically active cells are found the glands of the skin—the oil and sweat glands. The effect of x-rays is well shown in the former by their ability to lessen the output of oil in seborrhea and in acne vulgaris. Not every case of acne requires x ray therapy, and not every case treated should have the same dosage or length of treatment. Many patients do perfectly well with less than 75 r per week. Dark and oily patients and those in the older age groups are the most satisfactory patients for treatment. In acne, greater experience with radiation has reduced the dosage and defined the better types for treatment. Perhaps the percentage of cures is less, but greater safety has resulted.

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Hyperidrosis and bromidrosis also respond to radiation, but at times permanent relief may not be obtained. The central-nervous-system factor is one which may not be altered by x-ray, and care should be taken to limit the dosage to amounts which will not produce any permanent changes in the skin.

Not only in the treatment of glandular tissue is inhibition produced, but also in that of other tissues. With cells of the lymphocytic group, whether in the blood, as in leukemias, or in various tissues, as in infiltrations or chronic inflammatory process, x-ray has been proved to be extremely helpful. It is found in studies of cells exposed to x-ray that the chromosome in the nucleus tends to break up, and the protoplasm to liquefy, and when dosage is carried still further the cells themselves disintegrate relatively fast. This fact applies particularly to this group, so that numerous diseases, among them leukemia, mycosis fungoides, lichen planus and psoriasis, probably respond to radiation primarily because of such changes. It is not yet possible to cure Hodgkin's disease or leukemia or mycosis fungoides, but in many cases much comfort can be given to patients with these conditions. Change in the infiltration of lichen planus is a striking example of the effect of radiation on the cells present. In mycosis fungoides, in the early stages when the lesions are thin, small doses can be given, and frequently one finds that such doses produce a remarkable change so far as symptoms and manifestations are concerned. Later when there is much infiltration distinct granulomas appear, and perhaps when much radiation has already been given, the need for more intensive treatment and filtered treatment must be resorted to in order to keep pace with the manifestations of the disease and with the acquired resistance of the cells.

Again, in the benign types of epithelial hyperplasia the inhibitory effect of radiation is evident. In the verrucous type of lichen planus, certain warty growths and so forth, large doses, perhaps 100 to 200 r, with 0.5 to 1.0 mm of aluminum, at intervals of ten days to three weeks, are often more helpful than small doses at short intervals.

The inhibition of endothelial cells is well shown in the results of treatment of nevi and angiomas. The short wave lengths of radium are the most effective. With adequate filtration and care to avoid any reaction, angiomas shrink and leave no trace. It is possible that the filtered rays of high x-ray voltage may produce the same result, but the difficulties of application to restless children offer a serious disadvantage.

Another inhibitory effect of x-ray concerns hair. The growth of the hair at the base of the follicle

is inhibited, and after fifteen or seventeen days the hair begins to fall out, with subsequent regrowth in three or four months, provided that the physiologic amount was not exceeded. Many thousands of cases of ringworm and favus have been epilated without untoward results. Sycosis vulgaris also can be helped. Permanent epilation in hypertrichosis or hairy nevi should never be attempted. The experience of those treated according to the Tricho system is, of course, an argument against the use of x-rays for permanent epilation, but the dosage they received was probably excessive. The use of repeated epilation doses to the point of permanent epilation is a risky procedure, and eventually results in atrophy and its sequelae.

Inhibition has been discussed as the first of the physiologic effects of radiation, destruction may be considered as the second. The inhibitory action of radiation can be carried to the point of destruction. Here again the radio-sensitiveness of the various tissues is of importance. The doses of x-ray which will destroy cells of the lymphoid series, or cells with glandular activity or epithelial malignancy, are as a rule smaller than those required to destroy connective tissue or muscle. Therefore the destructive effect is most useful in the malignant type of tumors of the skin—carcinoma or sarcoma—and also in the granulomas of mycosis fungoides.

Cancerous cells must be destroyed! Biopsy and classification of the tumor in accordance with the standards worked out by Broders, the general condition of the patient and the site and tissue affected will indicate the method of attack and dosage. Six hundred to 900 r was formerly considered sufficient. The dose has gradually increased to 2000 and 2500 r or more, with various voltages and types of filtration, perhaps in one dose or in a series at short intervals. Such doses would have been considered radical a few years ago. Cases may be treated with a 100-kilovolt machine, using 1200 r unfiltered and 1200 r filtered with 1.0 mm of aluminum, a total of 2400 r, or with a 200-kilovolt machine, using 2000 r at one sitting, filtered with 0.25 mm of copper and 1.0 mm of aluminum. Excellent results are obtained with each, but it seems possible that the latter may produce somewhat better results in certain thick lesions and those with involvement of cartilage.

A third physiologic action of radiation is its antipruritic effect. Many itching dermatoses respond satisfactorily, but some do not. Many cases of thickened eczema, localized pruritus vulvae, pruritus ani and so forth are relieved. Senile pruritus very frequently is also improved. The itching and thickened dermatoses, such as lichen

planus, chronic lichenified eczema and mycosis fungoides, are also relieved. It has not been my experience that the itching of dermatitis herpetiformis or urticaria has been aided by direct radiation.

A fourth possible effect of the x-ray is the relief of pain. This is not highly regarded as an indication for radiation, but in the pain following herpes zoster one finds occasionally that x-ray helps. It has also been quite striking that many patients with verruca plantaris, within two or three days of intensive therapy, during which the pain may be slightly greater, are completely relieved of any sensation of pain. This relief and that from pain in inoperable cases of cancer are undoubtedly based on another effect of the rays.

A fifth physiologic effect cannot be stated so definitely. I refer to the effect of radiation on diseases caused by bacteria and fungi. Localized pyogenic infections, as well as various types of tuberculosis, are often greatly helped. Blastomycosis, actinomycosis, tinea barbae and fungous infections of the hands and feet respond to radiation. This is apparently not a direct effect on the fungus, because the destruction of cultures requires extremely large amounts of radiation yet very often pyogenic infections and infections from fungi respond extremely satisfactorily to proper doses of x-ray. The reason for the action in these diseases is not clear. It is possible that owing to the radio-sensitiveness of leukocytes they may be destroyed by the rays with the release of antibodies or ferments which are quickly available for defense against bacteria. It is also possible that an increase in phagocytosis is brought about by radiation. There is, altogether too frequently, a varying response in a given disease, and it is a question whether there may be more connective tissue in some cases and therefore fewer radio-sensitive cells. It is also possible that chemical changes are produced in the tissue which alter it and make it a less favorable place for the growth and action of bacteria. In the treatment of such cases filtered radiation seems to me to be more effective than unfiltered radiation.

CONTRAINDICATIONS

Factors in the Apparatus

In discussing the contraindications of dermatologic radiation one should first of all consider factors in the apparatus. Inadequately standardized apparatus constitutes a fundamental objection to radiation. Although an epithelioma may be treated without accurate calibration, extreme care is necessary for epilation, or the treatment of acne in a blonde, or even acne in general. Any change in the machine—the replacement of a

burnt-out tube, changing or overhauling the motor and so forth—requires careful checking in order to be sure that there has been no change in the amount of radiation delivered.

Another item of importance in this subject has to do with imperfectly trained technicians and assistants. The dermatologist should be absolutely sure that the technicians, assistants and graduate students to whom is entrusted the actual management of apparatus know the proper technique and are careful and accurate in carrying it out.

Idiosyncrasy

Idiosyncrasy has been mentioned as a possible item to be considered. True idiosyncrasy to x-ray is undoubtedly rare. An abnormal response to a relatively small dose has been found with other physical agents—heat, cold, ultra violet rays. The same type of response can be produced by x-rays and radium but these cases are unusual and their abnormal response to radiation can frequently be accounted for by other causes. Some of these causes have already been mentioned. Errors in technique, such as the omission of filtration, failure to measure accurately the target skin distance and imperfectly standardized apparatus such as I have just discussed are possible explanations. Wrong calculation in using the arithmetical measurement of dosage possibly explains some poor results. Failure of the voltmeter seldom occurs, but there should always be two millimeters in the circuit. Ionization measuring apparatus is a source of possible error both in the apparatus and in the calculation of roentgens per second. The lack of appreciation of the factors in the individual which influence dosage can often explain, in my opinion, some of the so-called cases of idiosyncrasy. Poor judgment in regard to disease and the patient to be treated decreases of course as a factor with increasing experience of the dermatologist in the use of radiation. Another contraindication is the lack of accurate diagnosis or the diagnosis of a condition not amenable to x-ray.

Previous Radiation

The history of previous radiation should be sought in every case in which the possibility of radiation is being considered. Under any conditions the physician should calculate and keep before him the total amount of radiation which the patient has received on a given area. The rule that not more than 4 skin units or 1200 r should be given to an area except in cancer is a safe one for the ordinary limit of radiation. But this limit has definite variations. It applies, I believe, to dark-complexioned, only skinned patients, but not to patients with blond skins or relatively dry skins or perhaps to treatment of the skin on

flexor surfaces I have seen cases in which even 2 skin units or 600 r should not have been given. All erythema must be avoided if possible, and if it does occur it must be considered as a possible contraindication to further treatment. The individual patient must be considered in attempting to define an upper limit, but the total dose should never be large enough to give rise to the possibility of later changes in the skin. All previous radiation should also be considered, even after a period of some years.

In addition to those cases which give a history of having had all the radiation they ought to receive, there is another large group in which it is impossible to ascertain the exact amount already given. There are many cases in which a roentgenologist or a clinic has been asked for this information, the reply gives the dose in terms of the various factors used, without indicating the amount required to produce erythema or epilation with that particular machine, or any indication of what these factors amount to. Arithmetical computation may give a very approximate dose, but for practical purposes one is faced with a patient who has had an unknown amount of radiation, and in general it is advisable to tell him that since he did not respond to radiation previously and has nevertheless had a recurrence, it is probably best not to treat him with any further amount.

Recent radiography is another factor to be considered. The fact that dental x-ray films are being so widely used makes it necessary to inquire in our acne cases with reference to a possible additional load of radiation from this source. Many of us have seen epilation or mild erythema produced on cheeks from repeated series of dental x-ray photographs.

Conditions Producing Erythema

In general it can be said that conditions which produce a dilatation of superficial capillaries add to the risk of radiation. One hesitates to treat acute inflammatory conditions of the skin. Some infections, namely boils and carbuncles, are definitely helped by a proper amount of radiation, but the acute inflammatory conditions, especially those arising from external irritants, should not be treated by x-ray until the acute phase has subsided, and in the subacute stage relatively small doses do best, with a very gradual increase to the proper dose.

Actinic exposure is another item to be considered. Erythema produced by exposure to natural or artificial ultra-violet light calls for extreme care in radiation. It is wise to caution acne patients in the spring to avoid sunburn, and if such occurs, to omit treatment or lessen the dose.

Various chemicals increase the clinical effect of

radiation in many cases, and radiation raises the threshold of erythema by these agents. Numerous lists of such agents have been published. They include iodine, tar, salicylic acid, chrysarobin, mercury, iodoform and sulfur, and it is possible that even a greasy coating over an area treated frequently may aid in exaggerating the effect of radiation. Extremely close consideration should be given to the coincident treatment of radiated areas.

Diseases with Atrophy

Diseases in which atrophy is characteristic or in which it is an end result are in general not suitable for radiation. I am well aware that carefully selected cases of lupus vulgaris or of lupus erythematosus have been treated successfully by radiation, but in general I believe that diseases associated with atrophy are much better treated by other methods.

Diseases Not Amenable to Radiation

X-ray and radium have been used in the treatment of almost every skin disease, but there are many diseases in which they have been found to be of no value. Some of the reasons can be assumed when the known physiologic effects of radiation are considered. These have already been discussed. It is found that such widely differing conditions as erythema multiforme, urticaria, benign tumors of various types, especially those with a large amount of connective tissue, parasitic diseases and a host of others are not candidates for radiation. Eczema which has failed to respond to previous radiation should not be further treated.

Psoriasis should, I believe, be included in the group of diseases not amenable to x-ray. It does, of course, respond to x-ray, at least for a while in many cases, but the cases must be carefully selected, and the treatment limited. I have probably seen more cases of post-radiation scarring, atrophy and telangiectasia in psoriasis than in any other single disease. The recurrence of lesions, persistent requests on the part of the patient for further radiation and inadequate standardization of apparatus in years past have been large items in the production of these sad results. There are many other diseases which experience has shown are not responsive to radiation.

Patients with Blood Affections

Finally, patients with severe blood or blood vessel affections are in general not candidates for x-ray therapy. Its effect on white blood cells and that on endothelial cells make it inadvisable in these cases. Indeed, in cases undergoing long-continued fractional treatment—those of mycosis fungoides, senile pruritus and so forth—white-cell counts

should be made from time to time in order to be sure that the number of cells remains within relatively normal limits during treatment

SUMMARY

If the skin diseases responding satisfactorily to radiation are carefully reviewed, it will be found that in almost all cases one or more of the following indications exist, namely the ability of the x rays to reduce cellular activity in glands, hair or other tissues, to destroy cells, to relieve itching or pain and to act favorably on certain infections.

There are also just as definite contraindications to the use of x ray in skin diseases. Inadequately standardized apparatus and imperfectly trained operators definitely contraindicate radiotherapy of any kind. In the individual case, previous radiation and in fact any previous recent therapy need to be carefully weighed. Conditions causing erythema call for deliberate judgment. Diseases associated with atrophy or certain blood or blood vessel affections and skin diseases found by experience not to be amenable to radiation constitute a group not to be treated. True idiosyncrasy is relatively rare.

If radiation seems indicated in a given case the following rules should be observed: be sure that the diagnosis is correct and that the possible contraindications have been reviewed, give close atten-

tion to the details of technic and be conservative in dosage except in cancer.

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DISCUSSION

DR. PHILIP COOK, Worcester: I should like to ask Dr. Lane whether he has had any experience with treating psoriasis over posterior nerve roots instead of directly over the area affected.

DR. ARTHUR M. GREENWOOD, Boston: I am in complete agreement with Dr. Lane. I had hoped that he would also discuss a subject which was recently considered at a meeting of the American Dermatological Association—the amount of radiation absorbed by the upper parts of the skin and the type of apparatus best fitted to deliver the desired radiation. The paper on this subject, by Dr. Cipollaro, tended to show that lower voltages were better suited to skin therapy than those above 100 kilovolts.

DR. LANE: In reply to Dr. Cook's question I am not prepared to express an opinion on treatment over the posterior nerve roots. I have attempted it but not with entire success. In my experience, cases so treated do not respond well.

In regard to Dr. Greenwood's discussion I too was very much interested in Dr. Cipollaro's paper, and particularly in the fact he brought out that there is so little difference between the depth doses of apparatus of voltages from 60 to 100 kilovolts. Dr. Cipollaro did some very careful work with reference to skin penetration and found comparatively little difference in the first two or three millimeters. Within that range the absorption is apparently sufficient to give adequate therapy with various voltages.

UTERINE PROLAPSE*

The Principle of Vaginal Approach, A Preliminary Report of 465 Interposition Operations

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WORCESTER, MASSACHUSETTS

WITH the warmth of deep interest and for two thousand years, we have fought over the problem of prolapse without reaching agreement on any one of the operations so far devised. And although it has been claimed in turn for each, it is doubtful whether any one procedure constitutes the final solution. But experience with them has given us, I believe, a fundamental operative principle, a principle which has few exceptions and which gives promise of holding true for some years to come. This is that at least after the menopause we can handle prolapse by vaginal operation alone, and without laparotomy. To a gynecological society this may sound

more like a platitude than a principle. However, the occasional operator notoriously, and my own colleague, the general surgeon, all too often call it heresy.

A principle so rich in practical results which is established but not accepted, can stand repetition and the cumulation of evidence. This paper reviews some of the existing evidence and adds that of a new series of interposition operations. The report of this series is preliminary and comparison between the interposition and other vaginal operations is purposely deferred. The comparison intended is that between abdominovaginal operations and a vaginal operation.

One might reasonably ask whether the amount of the work on prolapse and the heat of the debate are out of proportion to the gravity of the

Read before the New England Obstetrical and Gynecological Society May 23, 1928.
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lesion To think of prolapse as only a deformity or discomfort is to underestimate its importance Although spectacular complications such as strangulation and progressive ulceration of the prolapsed mass are too rare to be serious hazards in the given case, more or less distortion of the sphincters, urethra, ureters and bladder—some or all—occurs as a rule Clinically, one meets associated incontinence, frequency, burning and even acute retention Urologic studies made on many

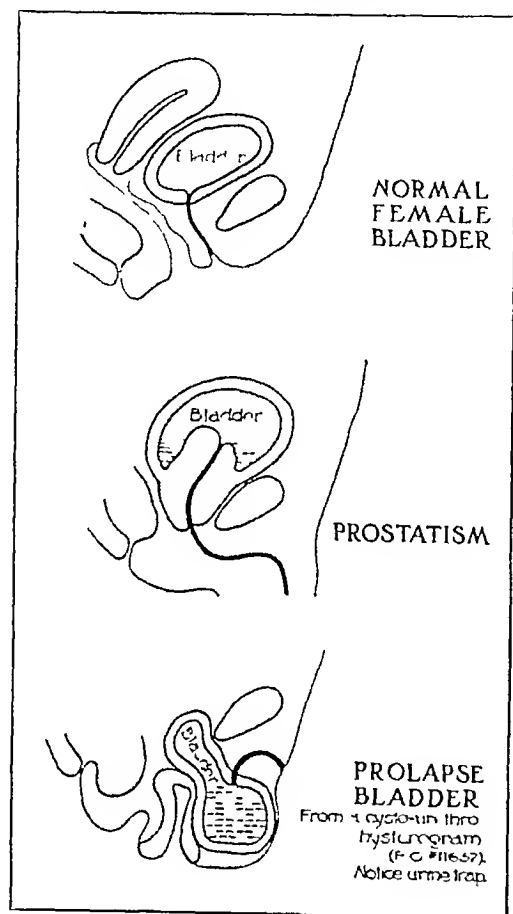


FIGURE 1

The Prostatism of Prolapse

of the recent patients in this clinic show a considerable incidence of obstruction and infection The bladder mucosa is usually injected, often thickened and sometimes as trabeculated as in prostatism There may be residual urine, hydro-ureter or hydronephrosis Renal function may improve after operation, as in prostatism Indeed it is not straining analogy to say that prolapse is the female analogue of prostatism (Fig 1)

THE PRINCIPLE OF VAGINAL APPROACH

The common operations for prolapse fall into two major groups the abdominovaginal, which combine vaginal plastic repair with some form of uterine suspension or fixation, and the all-vaginal

Abdominal hysterectomy is not an operation for prolapse The visible uterus is not the disease but only an evidence of the disease in the suspensory apparatus above Simple removal of it is quite comparable to amputation of an extremity for the pain of cord tumor and, incidentally, is followed by the most intractable recurrences

The three principal vaginal operations are vaginal hysterectomy, parametrial fixation (Fothergill or Manchester) and interposition In vaginal hysterectomy removal of the uterus is incidental, and the essence of the technic is the construction from the uterine pedicles of a shelf which is interposed between the bladder and abdominal viscera above and the vagina below The Manchester suspends the cervical half of the uterus in a sling made from the uterosacral ligaments and the bases of the broad ligaments Interposition, by drawing the fundus beneath the bladder and affixing it there, restores anteversion, changes the direction of the final component of intra-abdominal pressures and to some degree tightens the suspensory apparatus by contortion The posterior-wall repair which is combined with each of these operations returns the axis of the vagina from the vertical toward the horizontal If coitus need not be considered, complete vaginal closure (Dujarier and Larget) may be added to vaginal hysterectomy, or partial closure (Neugebauer-LeFort, Kahr) may be added to either vaginal hysterectomy, the Manchester or interposition *

It is the aim of all these operations to close a breach in the complicated line of defense across the pelvic outlet, which when open permits the condition that we inadequately call uterine or genital prolapse For a fuller discussion of the mechanics of pelvic support Farrar's¹¹ review and the mellow paper of Ward²² are recommended To summarize the subject arbitrarily, the upper ligaments of the uterus are negligible, but heredity and constitution, the hydrodynamics and aerodynamics, the leverages and the cleavage planes involved are of some importance, although they defy quick synopsis The fixed barriers to prolapse are a lower, supporting apparatus and an upper, holding apparatus The supporting apparatus is made up of the levatores ani and the muscular and fascial masses around the anal canal and lower vagina These back up the front line holding apparatus and come into action when parturition defecation or coughing threatens a break-through Damage to these structures is not so vital as it is at the upper level

*Kahr's²¹ refinement of a possibly prehistoric operation should be better known Essentially an exaggerated perineorrhaphy it joins the bulbospongiosus and the sphincter vaginae muscles across the posterior five sixths of the introitus leaving just enough space for the urethra to empty As simple as the Neugebauer-LeFort operation it avoids the drag on the anterior wall which is the presumptive cause of the incontinence occasionally reported after that operation

The upper, holding apparatus is idealized in Figure 2. It is a complex of tissues arising from the pelvic side walls and inserting all around the uterus at the level of the internal os. We confuse ourselves with names—cardinal ligaments, pubo-cervical fascia, pillars of the bladder uterosacral ligaments—applied to the parts of this structure that we separate at operation. And we de-



FIGURE 2. The Endopelvic Fascia (after Martin¹⁰)

The holding apparatus the first line of defense against prolapse. The uterus has been amputated at the internal os (int. os) which a tenaculum pulls aside. A V—peritoneum of anterior vault P V—peritoneum of posterior vault 1 2 and 3—the cardinal uterosacral and pubocervical ligaments respectively

ceive ourselves by the memory of the tenuous films which represent these tissues in the dissecting room. It must be emphasized that they are as different in vivo as is, say the biceps muscle.

Although the nomenclature of this holding apparatus and some of its anatomy are still debated its existence and its function can be easily demonstrated in the living patient. If one pulls down the cervix with a tenaculum a finger in the vaults feels this structure tighten as the uterine excursion stops. Furthermore, in hysterectomy the uterus and upper vagina remain relatively immobile until circumcision of the cervix releases them.

The basic pathologic anatomy of prolapse has to do with failure of this holding apparatus and less directly with the loss of uterine anteversion. Vaginal hysterectomy, interposition and the Manchester operation repair this apparatus. Abdominal suspension combined with the removal of pieces of vaginal mucosa does not. Provided that the vaginal part of the abdominovaginal operation repairs it adequately that is, if it approximates a Manchester there seems to be no need of adding laparotomy with its trauma pain and risk.

Instead of attacking the fundamental fault, abdominal suspension furnishes a substitute mechanism. It offers a crutch without setting the fracture. And the crutch is mechanically defective, for in recurrence after ordinary suspension the attenuated ribbon of uteroperitoneal tissue loosely connecting the site of the suspension to the prolapsed fundus bears witness that the function of uterine tissue is to stretch and not, as suspension presumes, to withstand stretching. The demands made on suspension by simple retroversion and those made by prolapse are not comparable. In retroversion, the operation merely holds in new balance a uterus the weight of which is borne by the pelvic floor. In prolapse, suspension assumes the dead weight of the pelvic floor and the organs on it transmitted through the uterus. Certain traumatic variations of suspension such as the suturing of a cut surface of the uterus into the rectus fascia after excision of the fundus or splitting of the body into halves, can presumably support such a burden. But I know of no evidence that they support it better than does transvaginal repair of the damaged holding apparatus. Furthermore, suspension is a notorious cause of pelvic discomfort and internal concealed and incisional hernias. I believe, therefore that it is not unfair to say that the abdominal part of an abdominovaginal operation helps but little and can do actual harm especially if the anticipated help tempts the operator to slight the important vaginal part.

These more or less theoretical considerations find support in two end result studies, chosen from the mass of such papers not for their partisanship but for their apparent detachment. The authors were, before the studies, outstanding champions of abdominovaginal operations, and had used them for the great majority of their cases.

Smith Graves and Pemberton¹ reported 530 prolapses of proclivity degree, that is with protrusion of the cervix through the introitus, treated by a vaginal plastic procedure combined with some kind of abdominal suspension. The mortality rate was 21 per cent the number of patients followed 439 with 273 followed two years or longer. The authors classified their vaginal plastics as complete or incomplete, depending on whether all or some of the operations of trachelorrhaphy (or cervix amputation) anterior colporrhaphy and perineorrhaphy were included. The study showed

In those cases where the incomplete plastic operation and abdominal suspension were performed about 70 per cent were anatomic cures and about 75 per cent were symptomatic cures. When the complete plastic operation and abdominal suspension were performed about 80 per cent resulted

in, anatomic cures, while about 84 per cent were symptomatically cured” Pemberton and his co-workers have since turned to all-vaginal operations¹⁸

The other study, by Frank, Lindeman and Maver, but reported by Frank¹² apparently included some cases of lesser prolapse, presumably cystocele or rectocele alone, or uterine prolapse of less than procidentia degree. Of 480 cases treated by abdominovaginal operation 414 were followed, 231 of them eighteen months or longer after operation. The results in these 414 cases were classified as follows: good, 46 per cent, adequate, 20 per cent, inadequate, 16 per cent, poor (including 10 per cent hernia), 18 per cent

prolapse. His cases are of unusual value because one operator performed them all, and did them under the hardest test of any prolapse operation: that of application of the operation to every prolapse. Unlike the Smith-Graves-Pemberton series, therefore, his included a scattering few of the lesser prolapses and, unlike many interposition series, some large and gigantic ones.

The follow-up, in which Drs. Jack Meyers, M. A. Bolger and Gerald J. Sullivan have assisted, has so far been done approximately two thirds by questionnaire and one third by examination. M. F. Fallon did 371 interposition operations, with a mortality of 27 per cent. Two hundred and fifteen of the patients have been followed two or more

TABLE 1 Interposition Results

YEAR	REPORTER	PLACE	NO. OF CASES	MORTALITY	NO. OF CASES FOLLOWED	SATISFACTORY RESULTS	COMMENT
				%		%	
1926	Johnson ¹³	Boston	140		100	81	
1926	Cron ⁸	Ann Arbor, Michigan	225	1—	183	95	13 operators
1926	Bullard ³	New York City			77	96	
1929	Broad ²	Syracuse	55	2	38	97	
1930	Calderon and Franco ⁴	Manila	28	0			
1930	Counsellor and Stacy ⁶	Rochester, Minnesota	71	0	59	96	
1931	Meshberg ¹⁷	Philadelphia	128	1—	92	92	
1933	Coventry and Moe ⁷	Duluth	76		70	98	
1934	Rongy et al. ¹²	New York City	501	1	398	95	8 operators
1935	Everett ¹⁰	Baltimore	242	1/2	149	89	Include previous papers from same clinic
1935	Cattell and Swinton ⁹	Boston	100+	2—	76	96	Include previous papers from same clinic
1936	Phaneuf ¹⁹	Boston	188	2/6		±90*	
1937	Baer et al. ¹	Chicago	121	1—	83	94	
1938	Fallon (this paper)	Worcester, Massachusetts	465	2/2	259	92	
	Collected cases		8302	2/2	4453	91/4	Langanki's ¹⁸ figures with corrections and additions

*Personal communication.

Frank called these results “extremely disappointing” and, like Pemberton, turned to the all-vaginal approach.

That these authors changed to the vaginal approach seems more significant than tabulated statistics. So many variables enter into end-result studies that few reported studies are strictly comparable. These variables are reduced, but not eliminated, in the following comparison of results after abdominovaginal and vaginal operations by limiting discussion to one of the three principal vaginal operations:

PRELIMINARY REPORT OF INTERPOSITION OPERATIONS

Although New England gynecologists until recently have favored the abdominovaginal operation, there have been nonconformists such as Johnson and his successors at the Carney Hospital, especially Phaneuf, and my father, the late M. F. Fallon. The latter turned to the vaginal approach in 1910, and for twenty years did the interposition operation routinely for postmenopausal

years, about 7 per cent had full recurrences, and 3 per cent had partial and for the most part asymptomatic recurrences. To the series can be added 94 more interposition operations of my own, done on selected cases of prolapses, with 1 death and no recurrences. Only 44 of my own patients have been examined after two or more years.

Table 1 summarizes some other series of interposition operations. Because of differences in one or more of the variables in end-result studies,—application of operation to all or only to chosen prolapses, modification of operation, number of cases, time and method of result determination, classification of results and the personal equation,—none of these are strictly comparable to the Smith-Graves-Pemberton or Frank series. The more important differences lie in the time and method of result determination and classification. However, the 259 cases in the two Fallon series which have been followed for two years or longer and checked by physical examination suggest that the com-

posite picture obtainable from Table 1 is not far from the truth

Although the study of the Fallon cases is unfinished, certain hazards and limitations, which are no fewer than, but different from those usually reported after interposition, have become manifest. For example, one of the commonest sources of criticism of interposition is its bladder complications, the so-called saddle bladder interposition bladder and so on, while little is said about the mortality rate. Yet the cases in our series so far have shown a negligible incidence of lasting bladder complications, possibly because at operation the bladder was adequately freed from the uterus. Our mortality rate of 2.2 per cent seems high, however, this rate is not exceptional, for, as shown in Table 1, the 8000 collected interposition operations gave no better results. But 2 per cent certainly seems high for a vaginal operation even though many of the patients be aged and infirm.

Listed below are the four chief faults I find with interposition, and some suggested countermeasures. The first two items on the list appear to be accountable for much of our mortality

First, actual interposition the pulling of the fundus through the anterior wall is usually done by tenacula, claw retractors or sutures which penetrate the uterine wall and may tear it in pulling down. The lacerations can be serious in themselves, and they also leave portals for later infection. After devising several instruments which I adopted a modified uterine sound with a bulbous end bulbous enough to prevent puncture, which pushes the fundus gently down from within. Secondly, interposition of the large, boggy atrophic fundus, in the M F Fallon series usually meant difficulty for the surgeon and discomfort for the patient, sometimes with recurrence or death. For some years, as reported to this society on July 4, 1932, we have irradiated (by radium) the atrophic uterus six months before operation so as to shrink and devascularize it. This has made operation easier and therefore safer and intellectually allowed better tailoring of the parts. Cause the uterus atrophies after interposition it is cut to fit a fundus the size of a fist will not the same fundus five years later, when it may be the size of a thumb.

Thirdly, interposition does not satisfactorily support the cervical stump. Since July 1935 for severe prolapses I have added a Manchester operation of the cervix. Judging from the results the 42 operations done by this method the combination promises well.*

Fourthly and finally, it is fairly commonly recognized

that interposition is not applicable to the woman who later may become pregnant. I believe we should widen this proscription and exclude the woman who is still menstruating. Pregnancy is only one of the many changes common before the menopause which, innocuous enough in a normally situated uterus, may set the scene for tragedy when the uterus is in interposition. The dysmenorrhea, the hematometra, the possibility of fibroids, the inaccessibility of the endometrium to the diagnostic curet and the dangers of hysterectomy of the interposed uterus all contraindicate interposition until menstruation has ceased and the common diagnostic problems of the menopause and the possibility of fibroids are past. Incidentally, interposition with tubal ligation has probably led to more induced abortions and disastrous deliveries than have been reported. But when the surgeon is confronted by a special premenopausal prolapse which he believes he can treat best by interposition it seems reasonable to do so and to produce the menopause by irradiation. It must be emphasized that, in this plan irradiation is not a mere contraceptive apart from the possibility of pregnancy, and even in the sterile woman I believe interposition should not be done until ovarian internal secretion has ceased. The rationale of this plan is the same as that which justifies irradiational menopause for fibroids or climacteric flowing or breast cancer. I have only twice used irradiation for this indication, because prolapse hardly justifies inflicting the premature menopause, whether by vaginal hysterectomy or by irradiation-interposition, when a lesser intervention would suffice.

SUMMARY AND CONCLUSIONS

Uterine prolapse is too often underestimated. Its urinary complications make it physiologically the analogue of prostatic disease. The essential lesion is a fault in the upper holding apparatus, which the principal all vaginal operations do, and abdominal suspension does not attack. End result studies support this and other a priori arguments for vaginal approach. The incidences of unsatisfactory results in the series of abdominovaginal operations which are quoted were 20, 30 and 34 per cent and in a preliminarily reported series of 259 cases followed after a vaginal operation (interposition) 10 per cent.

Since this paper is intended only to show that prolapse or at least postmenopausal prolapse should be handled by some vaginal operation, comparison of interposition with other vaginal operations is deferred but certain observations on interposition are reported.

Four hundred and sixty five interposition opera-

*This operation has since been proposed by Schumann (Surg. Gynec. & Obs. 191:446, 1939).

tions were done, with a mortality rate which was the same as that of 8000 collected interposition operations 2.2 per cent, seemingly high for a vaginal operation

An interposing instrument is advocated so as to avoid the trauma of tenaculum to the uterine wall

Interposition is dangerous and unsatisfactory when the uterus is large and metritic, but such a uterus can be prepared for interposition by irradiation

Interposition does not satisfactorily support the cervical stump, however, the Manchester operation, combined with interposition, does

Ovarian internal secretion, not merely the possibility of pregnancy, contraindicates interposition. The operation should not be done before the natural, or exceptionally an irradiational, menopause

390 Main Street.

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DISCUSSION

DR LOUIS E PHANEUF, Boston. Dr Fallon in his paper emphasizes the vaginal approach in the treatment of uterine prolapse. It has been my custom to divide prolapse cases into two groups: those women suffering from prolapse who are still young and who are susceptible to future pregnancies, and those afflicted with prolapse who have passed the menopause. In the group of young women the uterus is curetted and a trachelorrhaphy, an anterior colporrhaphy and a perineorrhaphy are performed. The abdomen is then opened, the uterosacral ligaments are shortened and the uterus is suspended. One of three types of suspension is employed, namely the Simpson suspension, the Baldy-Webster suspension or, rarely, the Olshausen suspension, the round ligaments being fixed to the abdominal wall with fine silk. The great majority of patients applying for the relief of prolapse fall in the second group, that is, women who have passed the menopause. In these patients I use the vaginal route entirely, as does Dr Fallon.

Since no one operation is applicable to all cases of prolapse, I have employed the following methods: interposition operation, vaginal hysterectomy with interposition of the broad ligaments, vaginal hysterectomy (clamp method) and anterior colporrhaphy, high vaginal fixation of the uterus, Fothergill or Manchester operation, and colectomy, subtotal or total. I have found that each of these methods has its place in properly selected cases. In all cases the perineum is repaired and the cervix amputated if lacerated, hypertrophied or irritated. The cervix is removed in all vaginal hysterectomies.

The interposition operation was described by Thomas J Watkins, of Chicago, in 1899. Frederick W Johnson, of the Carney Hospital, adopted it in 1902 and made it the operation of choice in that institution. I have used it somewhat more than any other method, having performed 199 operations. Recurrences have averaged in the vicinity of 10 per cent. A considerable number occurring after ten years were due to extreme atrophy of the uterus, the result having been satisfactory until this took place.

I have not used radium to reduce a large uterus before interposing it, having preferred some other method in the management of this condition. I believe that the interposition operation is contraindicated in the presence of a small atrophied uterus, because the bladder, by its greater weight, will again force out such a uterus.

As Dr Fallon has pointed out, the interposition operation should not be done before the menopause because of dysmenorrhea and occasionally menorrhagia and metrorrhagia, and because if it is used in young patients fibroids may develop, causing marked difficulties.

Recently, papers have been published from the Johns Hopkins Hospital and the Michael Reese Hospital, of Chicago, emphasizing the advantages of the interposition operation. In the latter institution they have gone back to the interposition operation, after having substituted vaginal hysterectomy for a number of years.

Any operation which conserves the uterus in the treatment of prolapse offers a decided advantage, should recurrence occur. It is more easily treated if the uterus has been retained than if it has not.

REPORT ON MEDICAL PROGRESS

CANCER

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THE *American Journal of Cancer* publishes annually about twenty five hundred abstracts of papers dealing with aspects of malignant disease. The Third International Cancer Congress, held in Atlantic City in September 1959 offered contributions from approximately five hundred participants. To attempt to summarize this furious activity or to survey as augur the hecatombs of rodents sacrificed in research is not only impossible but unwise. Any presentation must of necessity be superficial and selective.

EXPERIMENTAL CANCER

Chemical Compounds as Carcinogenic Agents

In an excellent review Cook and Kennaway¹ prepared a comprehensive summary of the literature for 1937 on this subject, adding a hundred and eighty new references to their already formidable bibliography. Undoubtedly even more work has been carried out in these fields in 1938 and 1939. Fieser has correlated carcinogenic activity with chemical structure in certain of the aromatic hydrocarbons. While such studies are invaluable to experimental workers the attempts to transfer the findings to clinical cancer problems are not very successful. Skin cancers occur in workers with tars and oils, mule spinners and chimneysweeps, cancers, bladder cancers in aniline workers, the lung cancers in the Joachimsthaler and Schneeberg miners and the osteogenic sarcomas in watch-dial painters are the outstanding examples of cancers due to chemical agents in man.

Hormones

Although the chemical relation of estrogenic hormones to some of the carcinogenic chemical compounds is striking the attempt to implicate them with carcinogenesis in man has thus far been unsuccessful. Shorr² stated "An analysis of the data leads to the conclusion that no evidence exists that estrogenic hormone, given in physiological doses, has led to the development of carcinoma in man." On the basis of the carcinogenic activity of estrogenic hormone in animals (Lacassagne³ and others) Gardner⁴ believes that the possibility of carcinogenesis by this means in man can

not be dismissed. "There is a great deal of evidence now available," he says, "that any chemical change causing prolonged proliferation of the cells of any type of tissue in the body may act as a carcinogenic agent." This statement obviously refers to the proliferative changes in the breast and female genital tract following administration of estrin.

Viruses

Although viruses play a prominent part in the etiology of a large number of animal neoplasms, they are not considered significant in relation to cancer in man. Andrewes⁵ concludes "There is no proof yet that a virus is concerned in the etiology of cancer in general. But there is evidence to make that idea worth very careful attention."

Genetics

While the geneticists have elaborated their conceptions of the genes responsible for heredity of carcinoma in experimental animals, and have gone so far as to identify two recessive genes, one for malignancy in general and another for organ localization (Slye⁶), Bittner⁷ by means of foster mother nursing experiments has demonstrated that the source of milk exerts a decided influence on the development of breast tumors. Mice nursed by low-tumor stock females showed a low percentage and mice nursed by high-tumor stock females had a high ratio of cancer incidence. This finding obviously calls for a revision of a considerable amount of the work on genetics which has been carried out and accepted as proved.

Other Experimental Studies

Andervont⁸ by preliminary implantation of a tumor in a rat's tail has been able to immunize the animal successfully against later implantation elsewhere in the body (after amputation of the involved tail). This immunity has been carefully studied but has not yet been explained. Brues⁹ has studied growth inhibiting substances, found in highest concentration in the liver and in part identified as aliphatic amines. He finds that in vitro they inhibit the growth of normal tissues more readily than that of malignant tissues. Fur

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ther work on cytotoxins and growth inhibitors promises developments of great interest

GENERAL CONSIDERATIONS

Educational programs designed to reach the public and the general practitioner have been sponsored by the American Society for the Control of Cancer, the American College of Surgeons and numerous other national and state organizations, both in the United States and abroad. These programs differ in detail and in scope, but all are directed toward the achievement of earlier diagnosis and better treatment. Lombard³ states that "cancer in Massachusetts is in the process of effective control," as shown by "a decrease in delay between the onset of symptoms and visit to physician first noted in 1936, a larger percentage of individuals consulting their physicians in the first month of the disease, an increased use of the tumor diagnosis service, a greater number of individuals with cancer utilizing the clinics, better teaching facilities, an extension of the co-operative cancer control committees, and a steadily decreasing adjusted death rate for females." In spite of this hopeful note, statisticians in general are convinced that cancer is increasing in prevalence, even when due allowance is made for age changes in the population.

Culpability for delay in treatment in a large series of cases was carefully analyzed by Pack and Gallo,⁹ and also by Kinney et al.¹⁰

An important series of studies by Nathanson and Welch¹¹ on incidence and life expectancy in carcinomas of various regions gives a clear conception of the natural history of the disease. Their curves, properly employed, should make it possible to appraise the efficacy of a method of treatment without the necessity of waiting the conventional five years for a follow-up study (Meigs and Dresser¹²).

DIAGNOSIS

Numerous biological and chemical tests for the presence of cancer continue to be offered by enthusiastic investigators. None of these seem to be of much value. Pfeiffer and Miley³ attempt to show specific alterations in the crystallization form of copper chloride when serum of a cancerous individual is added to the solution. They claim 80 per cent of positive tests in cancer cases, and 10 per cent of false positives in control cases.

Refinements in roentgenology have accounted for considerable improvement in cancer diagnosis, but they are too numerous to recapitulate here. Endoscopy, notably gastroscopy and pentoneoscopy, has improved the diagnosis in numerous cases. Aspiration biopsy (Martin and Ellis¹³) has many

supporters. Opponents point out the possibility of dissemination by this procedure. It is also emphasized that the amount of tissue secured is often inadequate even in the hands of expert pathologists. McLean and Sugiura¹⁴ carried out aspiration biopsies repeatedly on transplanted rat and mouse sarcomas without increasing the percentage of distant metastases.

TREATMENT IN GENERAL

Effective cancer therapy is still restricted to surgery, radium and x-ray. Improvements in surgery are chiefly technical, and deal with malignancy in special fields. The introduction of electrosurgery several years ago marked a distinct advance in the operation management of certain types of carcinoma. More recently the introduction of two active electrodes held close together has further improved this method of treatment. Improvements in anesthesia and in maintaining the patient's physiologic equilibrium have widened the scope of surgery and diminished its mortality. The use of zinc peroxide (Meleney,¹⁵ Sunderland and Binkley³) has made it easier to clean up foul and sloughing ulcerations.

However brilliant may be the technical advances in surgery, this method of treatment can be applied to malignancy only in an early and localized stage of the disease. Thus improvement in results of surgery, especially as concerns the total cancer problem of an anatomic region, must depend primarily on an educational program which will help to discover a greater proportion of the cancer cases in a stage favorable for cure.

A similar limitation of radical therapeutic effort to early and favorable cases does not apply to radiation therapy. Thus, advances in technology in this field carry the possibility of their application to a large proportion of the sufferers from a given type of cancer, including late neglected patients as well as those with early localized lesions.

Radiation therapy was recently reviewed in this journal by Dresser.¹⁶ The biology of roentgen therapy is still under investigation. Guyer and Claus and others have experimentally administered cobalt to animals before radiation in order to arrest cell division in the metaphase. They found that irradiation applied to the tumors was made more effective by this means. The attempt to adjust radiation dosage and intervals to the biology of the malignant cell probably accounts for the efficacy of the Coutard technic of radiation, as opposed to the single massive dose. Similar benefits also inhere in the Chaoul method of fractionated contact irradiation, as well as Pfahler's so-called saturation technic. The role of supervoltages in treatment is still under review. X-ray therapy

seems to be supplanting radium in some fields and platinum filtered radium needles have supplanted the use of radon seeds in many cases in which interstitial radium is employed. The use of radioactive isotopes (Lawrence⁹) is still a purely experimental field but one which is of great interest.

Laborde,¹⁷ writing on the subject of acquired radio-resistance, points out that the effect of radiation is on the host tissues rather than on the tumor itself. Hence resistance develops as the host tissues undergo changes in the vascular bed and fibrosis supervenes.

There have been reported some cases of pathologic fracture of the femoral neck following x-ray therapy which involved the pelvis and one such case has been observed at the Pondville Hospital. Numerous writers have reported studies of the pulmonary fibrosis which may follow roentgen therapy of the chest.

Smith and Fay¹⁸ have recently demonstrated the beneficial effect of local and general refrigeration as a palliative procedure. This work continues to be experimental, and will apparently require extensive physiological and clinical study before its efficacy can be determined. Other methods of pain control—sedatives, narcotics, neurosurgical measures and alcohol injections—have been effective in the vast majority of cases. Favorable reports have been made on the use of cobra venom for the relief of pain.

REGIONAL CARCINOMA

References to advances in the treatment of cancer of special regions have already appeared in this journal and no attempt will be made to cover the entire field. A few developments appear to be of special interest and will be recorded.

Cancer of the Mouth

Erf and Rhoads⁸ and Martin⁸ have made a careful study of vitamin B deficiency as it relates to precancerous and cancerous changes in the oral mucosa. Franseen¹⁹ has studied the Plummer Vinson syndrome as a precancerous condition presumably due to deficiency disease. Nathanson and Weisberger²⁰ have carried out therapy with estrogens in cases of oral leukoplakia, with considerable benefit. It is likely that these vitamin or hormone deficient states provide a favorable ground on which the chronic irritation of bad teeth and tobacco can excite cancerous changes. The high incidence of multiple oral cancers (Lund²¹) is in favor of such a theory.

Berven²² and Martin²³ both report excellent results on unselected series of mouth cancers by the use of intensive radiation therapy, with cures of 25 and 26 per cent respectively. Management of

the cervical lymph nodes is by means of watchful waiting, surgery in selected cases and usually radiation as well. Duffy⁴ has formulated the indications for cervical lymph-node dissection, and reports about 20 per cent cures in those cases with involved nodes which are subjected to radical dissection. Carcinoma of the lip has a much better prognosis, and is curable by neck dissection in nearly 60 per cent of patients who are subjected to operation with cervical node metastases (Taylor and Nathanson²⁴). Unfortunately, in both lip and mouth carcinoma many patients first present themselves with carcinomatous metastases which are already inoperable. In these cases radiation as advocated by Martin will occasionally effect a cure. Surgery following intensive radiation is extremely hazardous, as Dresser²⁵ has pointed out.

Thyroid Gland

In no field is the pathologist confronted with greater difficulty than when trying to correlate the histologic picture with the clinical course in thyroid malignancy. Vein invasion, histologically a malignant characteristic, is frequently a benign clinical condition. The presence of aberrant thyroid tissue and its tendency to malignant change are also confusing. In addition there is the likelihood of late recurrence, even after apparent cure has been effected. In general, treatment is by radical surgery combined with intensive radiation therapy. Ward³ reported cures in 30 per cent of a series of 95 cases subjected to operation.

An interesting epidemiological finding is the geographic relation between goiter and cancer in general (McLendon²⁶). This conclusion has been substantiated by other authors. There is no very satisfactory explanation of this correlation.

Larynx

Surgery, in the opinion of certain operators, continues to be the treatment of choice in small, localized growths in the larynx, however, the excellent results secured with radiation without mutilation seem to be an improvement on the results that can be secured by surgery.

Esophagus

Carcinoma of the esophagus is well nigh hopeless so far as cure is concerned. An increasing number of attempts at surgical extirpation are being carried out, and the field remains a challenge to the surgical virtuoso. Radiation has been disappointing in general as a cure although technical advances may improve the results. Excellent palliation is often secured by radiation. Bougienage is a hazardous procedure and of only ephemeral benefit. Painful and elaborate gas-

trostomies are devised, but they involve a considerable mortality and do not greatly prolong the life of the patient

Lung

There seems to be universal agreement that carcinoma of the lung is increasing. Ochsner³ insists that total pneumonectomy should be carried out in all operable cases, in order that a few lymph nodes may be removed. In the pathologic material which he analyzed 83 per cent of the cases presented regional node involvement. He also reported a mortality following pneumonectomy of 50 to 60 per cent. Since pathological confirmation of lung tumors is not usually available preoperatively, it seems unwise to advocate total pneumonectomy as a routine procedure.

Superior sulcus (Pancoast) tumors appear not to be a pathological entity. The syndrome associated with them is produced by the anatomic location.

Breast

Keynes²⁷ renews his interest in interstitial radium treatment of carcinoma of the breast, and results in his hands compare favorably with those secured by surgery. Recent sporadic impulses toward simple mastectomy in selected cases are retrogressive. The fallibility of clinical appraisal of axillary lymph-node involvement is sufficient argument to urge against the occasional efficacy of this method of treatment. Cures can be effected in 70 to 75 per cent of cases without axillary involvement, and in 25 to 30 per cent of cases with axillary involvement, by radical surgery alone (Simmons, Taylor and Welch²⁸), provided cases are properly selected. The arguments for preoperative or postoperative radiation are unconvincing.

Stomach

Balfour²⁹ reporting the Mayo Clinic experience with carcinoma of the stomach, gives a radical operability of 45 per cent, with an operative mortality of 14 per cent. Cures were effected in 48 per cent of the patients without lymph-node involvement and in 18 per cent in cases which had node metastases. These figures are more favorable than those secured by other surgeons. Total gastrectomy continues to be carried out in an increasing number of cases and perhaps an occasional cure may result. Lahey³ has recently re-emphasized the value of copious preoperative gastric lavage with dilute solutions of hydrochloric acid.

Colon and Rectum

Allen³⁰ recently commented on the excellent results reported in these fields by the use of Devine's method of preliminary colostomy. In general there seems to be increasing enthusiasm for two-stage radical operations on the colon. According to Dixon,³ the operability in colonic lesions is fairly high (71 per cent), the operative mortality in experienced hands is diminishing (20 per cent) and gross curability is fairly satisfactory (33 per cent).

The one-stage radical operation of the Miles type has become the method of choice for carcinoma of the rectum, with an operability of from 57 (Jones³) to 75 (Rankin³) per cent, an operative mortality of 7 per cent (both authors) and cures in the neighborhood of 56 per cent (Jones). Electrosurgical methods have been urged as a palliative procedure in inoperable rectal growths, without finding many enthusiastic supporters. Radiation is occasionally urged for these cases but has not proved helpful in most clinics. Studies on the spread of rectal cancer have been made by Gordon-Watson³¹ and Bacon and Gilbert.³²

Cervix

Schiller's test with iodine is now widely used to help detect suspicious areas in the uterine cervix, and an occasional early cancer may be discovered by this means. Colposcopy (Hinselmann) calls for great experience in interpretation of the appearances observed and has not achieved much popularity. Treatment seems to be tending toward standardization, with combined external roentgen therapy and intracavitary radium application. Divided and sustained radiation dosage seems to be better than single massive treatments. A few authors continue to advocate radical surgery in selected early cases.

The apparent relatively infrequent occurrence of carcinoma of the cervix in Jewesses is very interesting and calls for searching investigation (Auster³).

Functioning Adenomas

Great interest is shown in functioning adenomas of the ductless glands. The cases in general are rare, the syndromes are striking and results of surgical treatment are brilliant. Sometimes these tumors develop malignant characteristics, with death due to regional or generalized metastases. Studies of these patients shed more light on the functions of the ductless glands than on the etiology of cancer.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 25461

PRESENTATION OF CASE

A forty-two-year-old American chemist was admitted to the surgical service complaining of stomach trouble.

For five years before admission the patient had had attacks of abdominal pain accompanied by nausea, vomiting and occasionally diarrhea. These attacks first came at intervals of about six to eight months, and usually lasted from a few days to a few weeks, but they gradually became more frequent, and starting fourteen months before entry, they occurred once a month. These attacks had characteristically followed a definite course. Generally there was a premonitory phase of two or three days during which time the patient suffered from general malaise, marked anorexia and mild "gas pains." Following these early mild symptoms, lower abdominal, cyclic, steadily progressive, severe, cramping "gas pains" occurred every fifteen to twenty minutes. As the attacks persisted, the pains tended to become almost continuous and were then associated with nausea and vomiting. The latter usually brought relief. On some occasions an intestinal pattern was observed on the abdominal wall with the passage or "gurgle" of gas, this frequently disappeared, at which time the pains would cease. Often morphine and atropine hypodermically were required for relief. Profuse diarrhea usually followed these attacks. They were precipitated by eating foods with a high residue. Once the premonitory symptoms had appeared, however, the episodes could be aborted by a regime of mineral oil and a liquid diet. The last severe attacks occurred nine and eighteen months before admission. On these occasions there were no premonitory symptoms, the attacks were ushered in by chills, a rapid pulse, a temperature rise and sweating. The stools were never clay colored, tarry or bloody. There had been a weight loss of several pounds.

The patient was born and had lived most of his life in Massachusetts. Nineteen years before admission he had had influenza, which was followed by pleurisy, pneumonia and a cough said to be due to "chronic bronchitis." This cough with sputum continued for two years. At this time while running to catch a train he coughed up large quanti-

ties of blood. A diagnosis of pulmonary tuberculosis was made, and he was sent to a sanatorium where he remained for four years. His sputum was positive for tubercle bacilli at entry but soon became negative and remained so for his whole hospital stay, he was discharged thirteen years before the present entry. He seemed well until nine years before admission when he had another small hemoptysis. He sought no hospital treatment. One and a half years before admission the patient's sputum became positive. He was told that he had bilateral chronic fibroid tuberculosis with one or two small cavities, he entered another sanatorium where he remained until three months before entry. His gastrointestinal complaints were investigated while he was hospitalized. Two gastrointestinal series were done one year before admission, and both were described as negative. He entered here for further studies, for he thought that his gastrointestinal symptoms were not functional, as they had been described to him.

The physical examination revealed a poorly developed, undernourished man. There was dullness at both pulmonary apices, with bronchial breathing but no rales. Expansion was equal. Examination of the heart was negative. A freely movable tumor was palpated in the right lower quadrant. The rectal examination was negative.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. Blood examination showed a red-cell count of 4,600,000 with 80 per cent hemoglobin (Sahli), and a white-cell count of 11,000. Four sputum examinations were negative for acid-fast organisms. The serum protein was 6.2 gm per 100 cc.

Roentgenographic studies showed the ileum to be markedly dilated. It appeared that the entire cecum and a portion of the terminal ileum were intussuscepted into the ascending colon. A barium enema passed to the cecum without delay. The cecum was blunt and appeared shortened, and there was a filling defect at its tip about 4 cm in diameter. The tip of the cecum was opposite the crest of the ilium, and it was not possible to fill the terminal ileum, which was dilated and contained gas.

On the second hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR W. ALLEN: May we see the x-rays?

DR. GEORGE W. HOLMES: We have a series of x-ray films taken in the usual manner, some with the colon filled and others with it empty, and still others taken during fluoroscopic observation, the so-called spot films. There are one or two striking things in these films. First, as described

in the text, the cecum itself is never well filled. Secondly, there is some definite dilatation of the terminal ileum. Thirdly, there is this large filling defect in the cecum, which from our observations is quite characteristic of herniation of the ileum into the cecum. It changes a good deal in successive films: sometimes it is quite large, at other times small. A solid tumor within the cecum would not do that. It has to be a mass which moves in and out of the cecum. Then the brilliancy shows that it contains a considerable amount of gas. In some of the films, you can see a lobulated round mass within the ileum about the size and shape of a walnut, and there is no question it is in the ileum, not the cecum. We should interpret the finding then as a mass in the terminal ileum which produced a certain amount of obstruction and caused the ileum to be herniated into the cecum.

Dr. ALLEN: Without any question we have a man who had pulmonary tuberculosis. He also had an abdominal condition which had caused him a good deal of trouble in the five years prior to admission, and I suppose the first thing we should think about is tuberculosis of the cecum. On the other hand, Dr. Langdon Parsons has studied our cases of tuberculosis of the cecum and found a number of such patients who did not have tuberculosis elsewhere and who had no evidence of pulmonary tuberculosis. We might in other words, get one without the other. This man's story of recurring attacks of pain over a long period of time, not varying particularly in intensity until eighteen months prior to admission might indicate that the condition had changed during the past year and a half. Symptoms had been produced over a period of three and a half years by a high residue diet and relieved by a liquid diet plus mineral oil. This reminds us of a good many functional disorders that we have seen causing mild intestinal obstruction and brought on by a high roughage diet. A good example is seen occasionally in the diabetic patient who uses an excess of bran in his diet. In the South they have cases of intestinal obstruction from the residue formed from persimmons. This fruit grows wild and is considered to be delectable in season. The persimmon bezoar has become a well known entity in certain districts. These may pass the pylorus and produce intestinal obstruction. Several years ago we explored a man here for acute intestinal obstruction and found that 60 or 90 cm of the terminal ileum was packed with corn which he had obviously not masticated too well. In the hospital now there is a boy who has been operated on three times for small-bowel obstruction. At the last operation it was found that the obstruction

was due to a large quantity of apple pulp that the boy had not chewed well. So we can get intestinal obstruction from roughage alone. However, the other causes of recurrent attacks of obstruction have to be considered. Recurring intussusception is a very common one. We are told that this man may have had an intussusception, a statement which makes me a bit suspicious, but it is possible to have recurring intussusceptions at quite infrequent intervals, which are usually due to some tumor in the neighborhood of the ileocecal valve. I think Dr. Richard Schatzki has collected the intussusception cases in this hospital and reported some 18 or 20 cases in adults. He found that approximately half of them were on a benign basis, such as a benign lipoma in the wall of the large bowel or a polyp in the region of the ileocecal valve. Why Dr. Holmes called my attention to the tumor in the terminal ileum, I am not sure. It bothers me a little but must be considered. We also occasionally see cases of torsion of the cecum, a volvulus that produces temporary obstruction with spontaneous release.

One of course must always think of the possibility of recurring appendicitis in considering cases with repeated attacks of abdominal pain. It is difficult to account for the picture on this basis, however, because his symptoms had been so clearly mechanical until eighteen months prior to admission. The last two attacks were quite different. In these he had no premonitory phase. These attacks were ushered in by chills, a rapid pulse, fever and sweating. He insisted that his stools were never changed in character, so far as being clay colored or tarry and we have no history of diarrhea except after his earlier bouts of obstruction. The onset of abdominal pain and chills interests me a good deal because we studied the cases of postappendiceal pyelophlebitis that had occurred in this hospital and found that in every instance the initial attack of appendicitis had been started with a chill. We found however, that about 6 per cent of all cases of acute appendicitis started with chills. Inasmuch as the ratio of pyelophlebitis to acute appendicitis was only 1 to every 300 cases, it means that a good many cases of acute appendicitis may start with chills without developing pyelophlebitis.

We must think also, in relation to the chills and a palpable mass in the right lower quadrant of the fact that when carcinoma of the colon metastasizes to the liver, there is very apt to be a general reaction and chill. Occasionally one can date the time of liver involvement by that symptom. Also one would have to consider an abscess that had occurred and drained itself.

This man had no anemia. His blood was within

normal limits but that does not of itself rule out cancer of the right bowel, although we are more apt to see anemia associated with cancer of the right colon than we are with cancer of the left. However, we do see quite extensive lesions with no anemia. A slight leukocytosis does not tell us one thing or another. We should like to have known what his stools were like after admission to the hospital, and whether they were guaiac positive, but the record does not tell us that.

The question then comes down to differential diagnosis. We have a man with pulmonary tuberculosis, recurrent attacks of abdominal pain and a palpable tumor in the right lower quadrant. We have to consider a certain number of possibilities. Dr J. H. Means has pointed out that lymphoma must be considered in every case of differential diagnosis of tumor within the abdomen. I should expect if this were lymphoma that this mass would not have been so freely movable. I should expect that there would not have been this long history of five years, provided we can connect the early attacks with the later attacks. One must, of course, consider regional ileitis, a disease that may manifest itself over a long period of years and produce quite peculiar symptoms. One must also consider tuberculosis of the cecum, and I have considered it quite seriously. I very much doubt that this man had tuberculosis of the bowel, his symptoms have been too intermittent, and the tuberculous cecums that I have happened to see have not been so freely movable on palpation as this one was. One must, of course, consider recurring acute appendicitis with abscess formation, but it would be a very unusual form of appendicitis and I do not expect that it will prove to be that. Could a Meckel's diverticulum produce a situation in this region that would allow intussusception into the cecum? Dr Holmes points out that this little affair here looks quite like a Meckel's diverticulum as seen on a film, but one wonders how far this projection really is from the cecum and whether enough of the terminal ileum has been intussuscepted into the right colon to allow one to toy with the idea that it might be a Meckel's diverticulum. I wondered if it could be a polyp with a long stalk. I think it is not a polyp since the barium apparently outlines the inner side of it. A benign tumor in this region of course must be taken into consideration and that I believe is the commonest cause of chronic intussusception in the adult. Carcinoma in this region must be considered also, but I believe that this lesion was probably not malignant—at least it is fair to say that it could not have been malignant for five years

and still have been as freely movable as it appeared to be at the time of entry.

So I come down to hazarding a guess that this was a benign tumor of the terminal ileum, that it had for some reason or other produced chronic recurring attacks of intussusception, and that its exact nature would be impossible to determine until after operation.

DR TRACY B. MALLORY: Have you anything to say, Dr Holmes?

DR HOLMES: The question of Meckel's diverticulum was raised. I did not believe it was that. The general opinion in the X-ray Department was that it was a tumor in the wall of the ileum. We did not go any farther.

DR MALLORY: Dr Homans, have you ever seen an area of regional ileitis intussuscept into the cecum?

DR JOHN HOMANS: I cannot conceive of it being the cause of the stiffness of the wall of the bowel. I have an impression that some infection played a role here, perhaps superimposed on the original tumor. It might even have been an appendicitis of a sclerosing sort.

DR CHESTER M. JONES: Hyperplastic tuberculosis can give recurring attacks of obstruction with no intervening symptoms for intervals of many, many months, I believe. I do not know whether it would assume a form of tumor like this. I am somewhat inclined to doubt it, but I think this might be hyperplastic tuberculosis in one of its rare forms. One form of obstruction Dr Allen did not include is that caused by ascaris.

DR ERNEST M. DALAND: In going over this man's story we found that he had had pulmonary tuberculosis with apparent arrest of the tuberculosis from institutional care. He had not felt well for about seven years and had been unable to work more than a day or two at a time. He had been back to the sanatorium, and they believed that he did not have enough in the chest to make him feel as badly as he did. While there the last time he had several of these attacks but they usually came on after five o'clock in the afternoon or early in the morning. Many times he asked to have the house doctor come to see him in an attack, but by the time he was seen in the morning the symptoms had cleared up. There was that one important point—he had something that did not seem to be explained by pulmonary tuberculosis. This man went to the Baker Memorial Hospital for x-ray studies. The afternoon after the films were taken I saw him at my office, together with the x-ray report. At that time his symptoms had entirely cleared up, but it was suggested that he go immediately into the hospital. He waited three days, and when he entered, was

entirely free from symptoms. So we know that he had a recurring intussusception that did entirely clear up between the attacks.

He was operated on under spinal anesthesia and nothing was found except in the region of the cecum and the terminal ileum. The terminal ileum was very much thickened and dilated. About 12 cm. from the ileocecal valve was a circular ridge of lesions which we decided were tuberculous. The cecum was entirely replaced by a very large hard mass, much harder than we had suspected before operation. We were certain that the lesion was tuberculous, but whether or not there was a superimposed carcinoma we could not say. A lymph node was removed for diagnosis, and an anastomosis was done between the terminal ileum and the transverse colon.

He made a very good recovery except for a good deal of cough following operation. Thirteen days later a second operation was done, and the right colon was removed. At that time the pathological diagnosis of tuberculosis of the lymph node had been made, but even then we were not sure that we were not dealing with two processes. A right colectomy was done. He made a very good convalescence and left the hospital free from symptoms. His appetite came back, he returned to work as a chemist, has worked ever since, has gained weight and has been in good health.

PREOPERATIVE DIAGNOSES

Carcinoma of cecum?
Tuberculosis of cecum?
Recurring intussusception

DR. ALLEN'S DIAGNOSES

Benign tumor of the ileum with recurring intussusception
Pulmonary tuberculosis.

ANATOMICAL DIAGNOSES

Tuberculosis (hyperplastic type) of the ileum and cecum

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The specimen which came to the laboratory showed multiple areas of involvement with tuberculosis. The lesions were definitely nodular in type, with comparatively little ulceration, and may, I believe, be classified as so-called "hyperplastic tuberculosis." Several of these were clustered right about the ileocecal valve, and one nodule was 5 or 6 cm. up the ileum. There was one small area of involvement in the cecum but the major disease was in the ileum rather than in the cecum. I presume that the tu-

mor which Dr. Holmes described in the ileum was the upper, rather isolated nodule.

We used to think of intussusception as something that was virtually an act of God, perhaps that rather malign deity whom the insurance companies so frequently invoke, but in recent years, in adults at any rate, we have found that almost invariably the intussusception can be explained on the basis of some chronic underlying factor which in our experience has most frequently proved to be benign tumor, as Dr. Allen pointed out.

CASE 25462

PRESENTATION OF CASE

First Admission. A sixty-three-year-old Irish housewife was admitted to the medical service complaining of occipital headaches.

The patient regarded herself as well until seven and a half months before admission when she accidentally fell, struck the back of her head and lower spine and was unconscious for three hours. She remained in bed for the following two weeks, complaining of soreness and transient pain in the lower back. There was no retrograde amnesia or subsequent loss of consciousness. Six and a half months before entry she began to have head aches and profuse nosebleeds. The former were chiefly occipital but were also referred to the top of the head and the temples. They occurred with increasing frequency and intensity becoming daily usually in the evening. The nosebleeds were profuse, occurred several times weekly and characteristically seemed to relieve the dull aching fullness in the occipital region. During the six months before admission the patient had almost constant nausea but did not vomit, except on a few occasions when she raised swallowed nasal blood. The nausea resulted in anorexia so that she ate sparingly and lost 17 pounds in weight. During the present illness she had noted the gradual appearance of telangiectatic veins on her cheeks.

About five weeks before entry the patient developed an acute respiratory infection characterized by right chest pain, cough with rusty sputum, malaise, several chills and a temperature of 103°F. These symptoms subsided over a period of two weeks, but she did not regain her accustomed strength and as a result spent most of her time in bed. She felt "feverish" evenings and when seen in the Out Patient Department ten days before admission her temperature was 99.4°F. While kneeling to say her prayers nine days before entry she fell against her bed and received a black eye and a bruised shoulder. These subsided rapidly.

For four or five years she had had a sallow or "bilious" complexion as often as once a month, but no frank jaundice. The stools and urine were normal, and there was no pruritus. The patient had been married forty-five years and had had thirteen children, nine of whom were living and well. She had had seven miscarriages.

Physical examination revealed a well-developed and moderately obese woman who had a florid complexion and a protuberant abdomen. There were telangiectases along the sides of the nose and over the cheeks. The tongue was deep red but not smooth. The veins of the optic fundi were engorged, but the disks were normal and there were no pulsations in the vessels. There was a moderate kyphosis in the dorsal spine. The heart was not enlarged. There was a soft non-transmitted systolic murmur heard at the apex. Examination of the abdomen revealed a smooth, firm, non-tender, liver edge four fingerbreadths below the costal margin, with questionable shifting dullness in the flanks. An otherwise negative neurological examination showed a cogwheel rigidity in both arms, with a tendency to a slow, slight tremor in the arms and legs. The blood pressure was 150 systolic, 80 diastolic.

The temperature, pulse and respirations were normal.

Examination of the blood revealed a red-cell count of 4,860,000 with a hemoglobin of 111 per cent, a cell volume of 48.5 per cent, a volume index of 1.20 and a color index of 1.11, the white-cell count was 10,000 with 45 per cent polymorphonuclears. The specific gravity of the urine was never higher than 1.012. The stools were brown, formed and guaiac negative. A blood Hinton test was positive, a Wassermann test negative. A qualitative test for follicle stimulating hormone in the urine was positive. Two bromsulfalein liver-function tests showed 45 and 35 per cent dye retention. The serum nonprotein nitrogen was 16 mg per 100 cc, and the van den Bergh biphasic and slightly above normal. The Takata-Ara and formol-gel tests were strongly positive. A capillary blood-sugar tolerance curve read as follows: fasting 105 mg, one-half hour 156 mg, one hour and five minutes 178 mg, two hours 176 mg, three hours 144 mg and four hours 117 mg per 100 cc. X-ray studies of the esophagus, stomach, duodenum, chest and skull were negative. There was no enlargement of the liver. Intravenous pyelograms showed no evidence of disease in the upper urinary tract. Multiple diverticula in the transverse and descending colon were shown by barium enema.

The patient ran an uneventful hospital course with normal temperature, pulse and respirations

throughout. She tired of the numerous studies done on her and was discharged on the eighteenth hospital day with her work-up incomplete and her disease undiagnosed.

Final Admission (seven months later). A supplementary history obtained from the family physician revealed that the patient had drunk about 3 oz of whisky daily for six years. A few days after her hospital discharge she was given two injections of nearsphenamine by her physician. These were followed by chilly sensations, fever and malaise, without urticaria or bronchospasm. Three weeks later she developed jaundice after the third of six weekly bismuth injections. Four months before admission a three-week period of jaundice with "gall-bladder colic" appeared. Her physician stated that she had received no cinchophen, phenacetin or amidopyrine. From six weeks before admission until entry the patient became increasingly jaundiced. Her urine became the color of molasses, and her stools clay colored. Two weeks before entry her ankles and abdomen became swollen.

Physical examination was identical with that of the first admission, except that she was more undernourished, lethargic and deeply jaundiced, with numerous scratch marks and many telangiectases on the skin. The abdomen was protuberant and contained striae. Shifting dullness was present. The liver and spleen were not felt.

The temperature was 99.6°F, the pulse 100, and the respirations 35.

The red-cell count was 3,100,000 with 84 per cent hemoglobin, and the white-cell count 9900 with 77 per cent polymorphonuclears. The clotting time was ten minutes, the bleeding time three minutes (cuff and stab method). The urine examination showed a specific gravity of 1.018, with a +++ albumin, a ++++ bile and a negative sediment. The stools were brown and formed. The serum van den Bergh was 23.6 mg per 100 cc, direct. A bromsulfalein test showed 95 per cent retention, the total serum protein was 7.6 gm per 100 cc, the total cholesterol 49 mg.

The patient ran a steady, gradually downhill course, she became apathetic, then stuporous and on the fifth hospital day comatose and incontinent. She died on the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR THOMAS V URMY. This is a rather complicated case with several unusual features, particularly in the laboratory tests. I think that we shall make most rapid progress by attacking first the most prominent part of the picture—the very apparent disease of the liver. If we take the second entry alone, we have the typical picture of a failing liver, with an early exitus.

Going back over the history of the first admission we find that there are a number of facts which may be significant. In the first paragraph there is a statement that the patient had constant nausea for about six months before admission. We should be much more willing to ascribe nausea without vomiting to liver disease than to the reported head injury. There is also a note of telangiectatic veins in the cheeks. Then she acquired an acute respiratory infection, apparently pneumonia, following which she was less well and continued to run a low-grade fever for some time. It is very common in cirrhosis of the liver to see some intercurrent infection even a mild one, greatly activate the hepatic process fever may persist for several weeks. We therefore have every reason to suspect that she was suffering from cirrhosis which had been relatively asymptomatic until the pulmonary infection.

Physical examination the first time showed telangiectases, and the red tongue, not smooth, which is very often found in cirrhosis and is probably due to general nutritional deficiency. The liver was enlarged, and there was some question of ascites. Going on to the laboratory tests we find a high normal red-cell count for a woman, a very high hemoglobin and an elevated cell volume color index and volume index. In cirrhosis of the liver it is not uncommon to get this type of blood, with the exception that there is almost always an anemia. I cannot explain the absence of the latter but it is very unlikely that she had an Addison's anemia. The bromsulphalein test gives further evidence of liver disease, retentions of 45 and 35 per cent are consistent with cirrhosis. The serum nonprotein nitrogen was normal. The van den Bergh was not significantly elevated, but such a finding is not inconsistent with the diagnosis of cirrhosis. The positive Takata Ara and formol-gel tests are strong evidence in its favor. The blood-sugar tolerance test I cannot explain entirely. It was prolonged, as you would expect in a diabetic, and this raises the question of hemochromatosis. However, there was no further evidence of this disease. It may be that damaged liver function, with reduced capacity of absorbing glucose, was responsible for the prolonged curve, although I do not see why the fasting sugar should have been so high. The x-ray studies do not help. The esophagus apparently showed no varices although we do not know whether they were looked for. No enlargement of the liver was noted, although apparently it was easily felt on physical examination. I doubt if the liver had shrunk very much between the physical and x-ray examinations. The patient had a normal temperature in the hospital.

On the final admission we have much more

evidence pointing to liver disease, all of which is consistent with failing cirrhosis. Two toxic agents are mentioned. She had been drinking whisky daily and she also had received nearsphenamine, several weeks after which she developed jaundice. We know that two weeks before entry the ankles became swollen and the abdomen larger. At entry she showed lethargy, deep jaundice, apparent increase in the size of the abdomen and shifting dullness, all of which are typical of liver failure in portal cirrhosis. The liver was not felt this time, which is consistent with shrinkage in size. The fact that the spleen was not felt is not necessarily significant. At this time the red count was lower than at the first admission, which is consistent with cirrhosis. The color index was still high. The report on the urine examination is consistent with a failing liver, although we should expect to have seen many granular casts. The van den Bergh was naturally increased secondary to the intense jaundice. The bromsulphalein showed 95 per cent retention, a finding which is evidence of marked insufficiency such as that in acute yellow atrophy, if one can eliminate two other conditions, namely malignancy of the liver, in which case we should expect the liver to be large, and obstructive jaundice, which does not fit the history or various other findings, including the brown stools. The serum protein was 7.6 gm per 100 cc., which is normal. This is surprising because we expect the protein to be low in cirrhosis but if they had done the albumin-globulin ratio, I am sure that they would have found the albumin low and the globulin high as suggested by the formol gel test on the first admission.

A feature which is a little difficult to fit in is the story of typical gall-bladder colic (nausea vomiting and severe pain requiring morphine). However, this is not entirely inconsistent because cirrhosis of the liver may give severe pain in the right upper quadrant. Therefore though we can not eliminate the diagnosis of gallstones, I do not believe we need to assume it on the basis of the information at hand. The story of clay-colored stools following the attack is suggestive of common-duct obstruction, but at least after the patient reached the hospital we find that the stools were normal in color.

I cannot explain the very low blood cholesterol unless the figure is a misprint.

DR. JAMES T. HEYL. It was re-checked in the laboratory and again found to be 49, the lowest value on record.

DR. URMAN. I shall have to ask someone else to explain it.

It appears then that there was a portal cirrhosis

of the liver with acute failure in the last few weeks, no doubt in part precipitated by the administration of arsphenamine and the ingestion of alcohol. There is a possibility that a gallstone attack may have taken place, but I doubt it.

Two or three other things in the record should be discussed. The story of a fall with unconsciousness lasting three hours suggests a severe brain injury. There was no lucid period with subsequent loss of consciousness to suggest hemorrhage from the middle meningeal artery. There were severe headaches and nosebleeds coming on after a gap of one month. This combination usually raises the question of hypertension, but I doubt that a blood pressure of 150 systolic, 80 diastolic, could be called hypertension. In view of the head injury a month before, I think it is reasonable to assume the headaches were due to it. To be sure, dull headaches are not infrequent even early in the course of cirrhosis, but these headaches seem to have been more severe than one would expect in cirrhosis alone. The nosebleeds could have been a part of the generally increased tendency to bleed in cases of cirrhosis. I think we must assume there was some damage to the brain at the time of the fall and that it caused the headaches. The fact that the skull plate after admission did not show any abnormality, of course, does not rule out injury. The hospital neurological examination was not significant of anything more than mild paralysis agitans.

DR TRACY B MALLORY: Do you want to bring syphilis up at all?

DR URMY: I should have brought that up in connection with the headaches. Central-nervous-system syphilis would have to be eliminated, and she should have had a lumbar puncture for that reason as well as for investigation of the headaches per se. Syphilis could, of course, have played a definite part in the etiology of her cirrhosis. I cannot explain the reason for the follicle-stimulating hormone test.

DR MALLORY: Perhaps Dr Heyl will tell us why it was done.

DR HEYL: Dr Fuller Albright was interested in whether there was a Cushing's syndrome. She was studied completely from that point of view.

DR HOLMES: In the x-ray films there are two or three things that in a negative way are of interest. I am always interested to see of how much value x-ray study is in determining the size of the liver. On physical examination the liver was said to be large, this was denied by the roentgenologist. In this film you can see the edge of the liver very distinctly here, and it is about opposite the twelfth rib posteriorly, so it seems as if it could

not have been very large. The films of the skull are negative, but I should agree with Dr Urmy that that does not mean anything. One other interesting thing is that diverticula sometimes show up much better after the colon is emptied than they do when it is full.

DR WILLIAM B BREED: Dr Urmy, would you not be willing to reject Dr Mallory's sly suggestion of syphilis? You seemed rather inclined to accept it partially. The only pertinent information we have is a positive Hinton test, a negative Wassermann test, many living children and several miscarriages. The fact must be remembered that syphilitic cirrhosis is a very unusual occurrence. I think it would be interesting for us to give Dr Mallory a definite answer to the question, or at least an opinion. I should be willing to say that syphilis had not played a part in this woman's disease. Can we find what the impression about her was in the wards?

DR HEYL: As I remember it we had the impression that she was suffering from acute liver insufficiency, the three possible causative factors being arsphenamine, alcohol and syphilis, and that she died a death of severe liver insufficiency. We thought her liver must be small.

CLINICAL DIAGNOSIS

Subacute yellow atrophy of the liver, with liver insufficiency

DR URMY'S DIAGNOSES

Portal cirrhosis of the liver, with acute failure
Head injury—type unknown

ANATOMICAL DIAGNOSES

Cirrhosis of the liver, old, type undetermined
Subacute atrophy of the liver
Jaundice
Ascites
Diverticula of the colon
Hirsutism

PATHOLOGICAL DISCUSSION

DR MALLORY: I wish I could answer some of the questions brought up by this case more definitely than I can. She certainly did not have a very large liver at the time of autopsy. It weighed just under 1500 gm., which is within the normal range for a woman. It showed, however, a very wrinkled, lax surface, and it cut with considerably increased resistance. On microscopic examination there was an obliteration of the normal architecture, a great deal of fibrosis which looked quite old and, finally, extensive, in fact almost complete, fresh necrosis of the remaining liver cells.

My guess would be that we were dealing with a fairly acute atrophy of a liver that was previously cirrhotic. That is perhaps too long a guess considering the limited amount of evidence that we have. If we assume that we are correct in supposing pre-existing cirrhosis, I am sure I do not know what it was other than portal. There was nothing to suggest that syphilis played any part in the picture. I think we should all like to know whether 3 oz of whisky a day for six years was significant. I cannot answer that question. I think we have to attribute the terminal attack to the arsphenamine or the bismuth or both. The jaundice that is so commonly seen under those conditions must be attributed to liver damage, and I for one am sure that it may on occasion lead to atrophy. It is not unreasonable to suppose that the hazard is greater in a person with an already damaged liver, although the whole event can happen, I believe, with livers normal at the time the arsphenamine is started. She had no gall bladder disease, no stones. The skull and brain were entirely negative. There was no evidence of a sig-

nificant traumatic lesion. The pituitary and adrenal glands were both negative, thus ruling out any question of basophilism.

DR. HOLMES: Was the spleen enlarged?

DR. MALLORY: It was normal in size, weighing 125 gm.

DR. HOLMES: There was no evidence of varices?

DR. MALLORY: The man who did the examination thought he saw some minute varices. It is very difficult to be sure of small varices at autopsy. In the face of a normal sized spleen I think the observation is doubtful.

DR. BREED: How toxic is bismuth to the liver?

DR. MALLORY: The rather common observation seems to be that the patients who are treated with arsphenamine sometimes develop jaundice immediately but perhaps a little more frequently later, at a time when they are very apt to be getting bismuth. I believe the consensus is that with bismuth alone jaundice is very unusual. Can you answer that, Dr. Short?

DR. CHARLES L. SHORT: I should agree with what you have said.

The New England Journal of Medicine

Formerly the

Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

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THE NEW HAMPSHIRE MEDICAL SOCIETY
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SUBSCRIPTION TERMS \$6.00 per year in advance postage paid for the United States Canada \$7.04 per year \$8.52 per year for all foreign countries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon on Saturday

THE JOURNAL does not hold itself responsible for statements made by any contributor

COMMUNICATIONS should be addressed to the *New England Journal of Medicine* 8 Fenway Boston Massachusetts

MEDICINE AND THE PRESENT CRISIS

For several years the Four Horsemen of the Apocalypse, mounted upon the steeds of Conquest or Plague, War, Famine and Death, have ravaged Asia and parts of Europe. Fear of the spread of their influence to the total involvement of civilization as we know it has been the concern of thoughtful men and women throughout the world, and the course of history during the past year has shown such fear to be well founded.

A crisis, then, exists, whether or not we choose to admit to ourselves its influence, immediate or remote, on our lives. Unpredictable and well-nigh incredible events have recently followed one another in rapid succession. Freedom of thought, speech and action in many parts of the world is

on the defensive against the assaults of both political and ideological tyranny.

Medicine is no less influenced by the trends of world affairs than any other human activity. Although the ideals which it professes and the scientific foundations on which it is based are limited by no international boundaries, it is nevertheless true that both of these attributes may, under certain conditions, take divergent courses and pursue different purposes on the two sides of a hostile frontier. Although today, by the grace of God, medicine in the United States is not behind a hostile frontier, it should, like the nation of which it is a part, carefully survey and deliberate on its course in an uncertain future.

For the present two duties are apparent. The first lies within the realm of enlightened and patriotic self-interest, the second within the scope of professional relations. Both require study and application.

The vitality of a democratic society or nation on which its survival is based, is derived from individual intelligence, realism and courage. The possession of one of these qualities without the other two, or of two without the third, does not suffice. That society or nation which is endowed with the highest intelligence will select the wiser course, provided it use realism to reject the appeal of prejudice, emotion and biased information (commonly known as propaganda) with which its intelligence is always assailed in times of crisis, the course thus selected, if adhered to with courage, will yield the most certain prospect of survival in an uncertain world. Medicine in the United States, although numerically but a small part of the nation which it serves, ranks high in the level of its intelligence. It should, however, study both world and national affairs, and by refusing to be led astray by prejudice, emotion and biased information attain the highest possible degree of realism. It should, both individually and collectively, place its reasoned opinions before the government which it has helped to create. Though there may be some who do not believe in the motto, *Vox populi, vox dei*, it is nevertheless true that the more audibly, intelligently and realistically

ly the voice of the people is kept before the government which it has created to conduct its affairs and to guard its interests, the more nearly is achieved the ideal of a government of laws and not of men. Therefore alert, intelligent, realistic and courageous citizenship becomes the first duty at all times of the American physician and American medicine.

In the realm of professional relations the duty of medicine is no less clear. The healing art is designed to restore to health not only the diseased body and the deranged mind, but also to guide the emotions under control of the intellect. If medicine, by its moral and civic example, and by its therapeutic precepts, can instill into those to whom it renders service not only physical health but also emotional balance and clarity of perception and reasoning it will have done its duty amply in preparing our country for any adjustments or hardships which the future may bring.

RED CROSS MEMBERSHIP

Red Cross membership serves a double-barreled purpose. From the rosters of those who annually join the organization during Roll Call are drawn the volunteer workers who conduct most of the organization's work. From membership dues it derives the funds needed to carry on its day-to-day activities. Only in times of great disaster are special contributions and gifts requested.

During the past year Red Cross volunteers produced 720,000 pages of Braille reading matter for the blind. In some cases these pages were printed from aluminum or other plates, necessitating presses, in others each page was made up individually. Special paper had to be used. Each page had to be coated with a special shellac. Volumes had to be bound. Each operation cost a small amount. When costs are multiplied by 720,000 the result is a sizable figure.

Other Red Cross volunteers during the year produced 330,000 garments for disaster victims and others in need. In many cases the cloth had to be bought. The garments had to be sewed, necessitating sewing machines, needles and thread. The

net cost of each garment was not great, but 330,000 such garments represent a considerable expenditure.

During the past year full-time professional public health nurses employed by the national organization and its chapters made more than 1,000,000 visits to or on behalf of the sick and examined thousands of school and pre school children. The cost of each visit and each examination was comparatively negligible but by the time that figure is multiplied by more than one million, the sum runs into six figures.

Likewise 313,000 persons received instruction in first aid to the injured, another 100,000 were trained in water-rescue methods, and 2720 highway emergency first aid stations and 2424 mobile first-aid units were being maintained as of July 1. During the year 40,000 men in the active armed forces of the United States, 165,000 veterans and 116,000 civilians, or families and dependents of these three classifications, were provided assistance in presenting government claims, in readjusting themselves to new conditions and in meeting various forms of distress. Again, each person trained in first-aid and water rescue work, each first aid station or unit, or each individual or family assisted, represents a comparatively small outlay, but when these numbers run well into the hundreds of thousands it requires no imagination to see that their ultimate total annual cost mounts into money.

There are many other avenues along which the Red Cross combats human suffering. Anyone will realize there is no particular limit to its activities. Allowance must be made, not only for their continuance, but for their expansion. This growth of Red Cross services can only come with an increased membership—more members to volunteer their services in unselfish devotion to humanity, more members whose annual dues, though individually small, will finance continued growth of the Red Cross.

Besides the need of providing for Red Cross expansion, the present world uncertainty may bring great humanitarian problems. Though charity begins at home and the primary obligation of the Red Cross is to American citizens, Norman H

Davis, the organization's chairman, has said "The American Red Cross must, within the limit of its resources, extend aid to the victims of disaster in the world neighborhood in which we live. Charity is not worthy of its name if it ends at home."

It is for these reasons the Red Cross this year has set itself to enroll 1,000,000 additional members. Out of a population of 130,000,000 it is seeking some 6,600,000 who believe in extending a helping hand to those less fortunate than themselves. The annual Roll Call, when chapters the country over issue an invitation to join their ranks and thus enable the Red Cross not only to keep abreast of demands, but to prepare for any emergency, began November 11 and ends November 30.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

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330 Dartmouth Street
Boston

SEPTIC ABORTION

Mrs. M., a twenty-seven-year-old para II, entered the hospital on the morning of July 31, 1939, when about ten weeks pregnant. She had begun to flow a little on June 28 and had been flowing bright blood every day since July 1 sufficient to require at times the wearing of a heavy bath towel.

The family history was noncontributory. The patient had had mumps, measles and chickenpox. In 1937 she had had scarlet fever. An appendectomy had been performed in 1930. Catamenia began at twelve, were regular with a twenty-eight-day cycle and lasted four days. Her last period had begun on May 14. Her previous pregnancy, six years before, had been normal in every respect.

Examination on entrance showed a well-developed, very pale woman. The heart was not enlarged, there were no murmurs. The lungs were clear and resonant, there were no rales. The abdomen was soft, with a right-rectus appendectomy scar. Vaginal examination showed the fundus to be retroverted and enlarged. There was some fresh bleeding. The temperature on admission was 100°F, the pulse 80.

The afternoon temperature on the day of entry

was 102°F, the pulse 100. She had a chill that night with a temperature rise to 106°F and a pulse rise to 140. The next morning the temperature was 100°F, but in the afternoon rose to 104 with a pulse of 120. She continued to bleed freely, and on August 2 she was transfused with 500 cc of citrated blood. She was seen in consultation, and a diagnosis of septic abortion was made. Because of the continued bleeding, exploration of the uterus was advised. Although the temperature following another chill had risen to 105°F, this procedure was carried out on August 4. At the time of operation she was given a second transfusion, consisting of 500 cc of citrated blood. The uterus was explored digitally and a considerable amount of adherent placental tissue was removed, the bleeding promptly ceased. The temperature came down to normal the following day and remained normal.

The red-blood-cell count on August 1 was 3,400,000, and the hemoglobin 70 per cent. On August 4 before operation the red-cell count was 2,200,000, the hemoglobin 48 per cent. Blood cultures showed no growth. Vaginal cultures on two occasions showed a few colonies of *Staphylococcus aureus* and moderate number of *Bacillus coli*. The cultures from the uterus at the time of operation showed *Staphylococcus aureus*.

She remained in the hospital for five days after the operation and was discharged relieved at the end of that time.

Comment. This case represents the ideal treatment for a septic abortion complicated by hemorrhage. Although the temperature was ranging from 100 to 105°F, the uterus was left alone until continued hemorrhage made its invasion necessary. The patient had bled so much before entering the hospital that a transfusion was done two days later. In spite of this transfusion her red-cell count on the morning of operation had fallen to 2,200,000 from 3,400,000. The routine of starting transfusion at the time of the operation is worthy of note. During the operation considerable blood was lost, which was immediately made up for by the transfusion. The invasion of the uterus was carried out because of hemorrhage and done in the gentlest manner possible. The handling of the case from the beginning to the end was ideal.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning November 20.

BARNSTABLE

Sunday, November 26, at 4 00 p.m., at the Cape Cod Hospital, Hyannis. Syphilis in Pregnancy and

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

the Offspring Instructor William P. Boardman. Donald E. Higgins, *Chairman*

BOSTON NORTH

Thursday November 23, at 4:00 p.m., at the Morton Hospital, Taunton. Pneumonia. Instructor W. Barry Wood, Jr. Lester E. Butler, *Chairman*

BOSTON SOUTH (New Bedford Section)

Friday November 24, at 4:00 p.m. at St. Luke's Hospital, New Bedford. Cardiovascular Disease. Eleven important questions about heart disease and their answers. Instructor Bernard J. Walsh. Robert H. Goodwin, *Chairman*

BOSTON NORTH

Friday November 24 at 4:30 p.m. at the Lawrence General Hospital, Lawrence. Common Problems of Neurology. Indications for lumbar puncture. Instructor T. J. C. von Storch. John Parr, *Chairman*

BOSTON SOUTH

Tuesday November 21 at 4:00 p.m., in the Conference Room of the Salem Hospital. Salem. Convulsions in Infants and Children—Etiology and Treatment. Instructor John A. V. Davies. J. Robert Shaughnessy, *Chairman*

MIDDLESEX EAST

Tuesday November 21 at 4:00 p.m., at the Melrose Hospital, Melrose. Gonorrhea in the Female. Instructor Alonzo K. Paine. Walter H. Flanders, *Chairman*

MIDDLESEX NORTH

Friday November 24, at 4:45 p.m. at St. John's Hospital, Lowell. Head and Spine Injuries. Instructor Walter R. Wegner. William S. Lawler, *Chairman*

WORCESTER (Milford Section)

Tuesday November 21 at 8:30 p.m., in the Nurses Home of the Milford Hospital. Milford. Common Problems of Neurology. Indications for lumbar puncture. Instructor H. Houston Merritt. Joseph Ashkins, *Chairman*

WORCESTER (Worcester Section)

Friday November 24, at 8:00 p.m. in the Staff Room of the Worcester City Hospital, Worcester. War Gases. Instructor G. Philip Grabfield. George C. Tully, *Chairman*

WORCESTER NORTH

Friday November 24 at 4:30 p.m., in the Nurses Home of the Burbank Hospital. Fitchburg. Convulsions in Infants and Children—Etiology and Treatment. Instructor Louis K. Diamond. George P. Keaveny, *Chairman*

DEATHS

HALLETT—EDWARD B. HALLETT, M.D., of Gloucester died November 8. He was in his seventy-sixth year. Born in Yarmouthport, he received his degree from Dartmouth Medical School in 1887 and served his internship at the Chelsea Marine Hospital. He settled in Gloucester fifty-one years ago and until five years ago was port doctor for the United States Public Health Service. Dr. Hallett was a former president of the medical staff of the Addison Gilbert Hospital in Gloucester. He was a member of the Massachusetts Medical Society and a fellow of the American Medical Association. His widow, a son Dr. Ronald P. Hallett, a daughter and a sister survive him.

PAGE—PETERSON S. PAGE, M.D., of Andover died May 23. He was in his sixty-eighth year.

Born in Williamsport, Pennsylvania, he attended the University of the State of New York and the International Y. M. C. A. Training School in Springfield, Massachusetts. In 1899 he received his degree from University and Bellevue Hospital Medical College.

Dr. Page was master of physical education at Phillips Academy, Andover, having held this position since 1902. He helped to build the school infirmary in 1912 and before he died a new addition to it was completed largely under his direction.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and four daughters survive him.

MISCELLANY

DIRECTORY OF MEDICAL SPECIALISTS

The Advisory Board for Medical Specialists will issue in December the first edition of the *Directory of Medical Specialists* listing approximately 14,000 specialists certified by the twelve American boards and the two affiliate boards.

This directory will have three sections. The first will be devoted to a brief discussion of the Advisory Board for Medical Specialists, its organization and objectives. The second section will have fourteen separate divisions, one for each American board, with a geographic and a detailed biographic listing of its diplomates. Each of these divisions will give full information regarding requirements for admission to examinations for certification, details of organization of each board and other general information. The third and final section will be a complete alphabetical list of all 14,000 diplomates, with their addresses and indications of specialty certification.

It is expected to issue the directory every two years. No charge is made for listing in the directory and only the names of the specialists certified by the American boards will be included. The directory represents an effort officially to inform the lay and medical public regarding the present strong movement for certification of qualified medical specialists.

Financial support has been given the directory by the American boards. The project is not designed to be profit making, and the widest possible public distribution of the directory is desired. On these accounts, the subscription price of the book has been set at a sum (\$3.50 per copy) computed to cover only publication expenses.

The directory should be invaluable to the entire medical profession in the reference of patients, as well as to many other ways and the individual support of this new project of the American boards is earnestly solicited of every diplomate. The directory will be sold generally to physicians, libraries, hospitals and others by subscription. Such subscriptions may be made through the Columbia University Press, 2960 Broadway, New York City or through the office of the directing editor, Dr. Paul Titus, 1015 Highland Building, Pittsburgh, Pennsylvania.

NOTE

Dr Charles T Porter, of Boston, was elected third vice president of the American Academy of Ophthalmology and Otolaryngology at the recent annual meeting in Chicago. Among the appropriations for research was one of four hundred dollars to Dr Moses H Lurie, instructor in otology, Harvard Medical School, for studies on the balancing apparatus of the ear.

CORRESPONDENCE

CANCER AS A PUBLIC-HEALTH PROBLEM

To the Editor In the editorial on "The National Cancer Institute" in a recent issue of the *Journal* you gave credit properly to the late Drs G H Bigelow and R B Greenough for splendid work in the early days following the recognition of cancer as a public health problem in the State of Massachusetts. You neglected, however, to refer to the pioneer work of Dr Francis D Donoghue, who was largely responsible for legislative action establishing the Pondville Hospital under the Massachusetts Department of Public Health over the protests of many public-health authorities. I am sure that the failure to refer to Dr Donoghue's part in this work was an oversight which should be corrected.

TIMOTHY LEARY, M.D.

784 Massachusetts Avenue,
Boston, Mass

TELEPHONE RATES FOR PHYSICIANS

To the Editor I enclose a copy of a letter from Mr Ash of the New England Telephone and Telegraph Company, which I believe will be of interest to the readers of the *Journal*.

ELMER S BAGNALL, M.D.

281 Main Street,
Groveland, Massachusetts

Dear Dr Bagnall

I am very glad to outline, as you recently requested, the regulations regarding the application of business or residence telephone rates for physicians.

Business rates usually apply for telephone service installed in the office of a physician, surgeon, dentist, veterinary surgeon, chiropractor, osteopath or other medical practitioner or of a clergyman or Christian Science practitioner or other persons actively engaged in a professional pursuit, when the office is used for the business purposes of the individual or of the organization with which he is connected, whether the office is located in the residence or in another building. When a practicing physician is not a subscriber to or joint user of business service, or a habitual user of it at another location, as at a hospital, there is a presumption of substantial business use of the service in his name at his residence, although such circumstances cannot be considered conclusive.

When a listing is requested containing a word or an abbreviation clearly indicative of the subscriber's profession (physician, dentist and so forth) it should be considered that the applicant has definitely stated that the use of the associated service at his residence is primarily for occupational purposes and business rates apply. However, a simple abbreviated title such as is ordinarily used in addressing the individual concerned, for example, "Dr" or "Rev," is not considered as clearly indicative of a substantial occupational use of the service, and if the

use of the service at the residence is primarily for social or domestic purposes, residence rates apply. When the listing contains such a title and the subscriber admits that the use of his service is primarily for occupational purposes or when he does not concede this fact but the evidence clearly indicates that this is the primary use of the service, business rates apply.

DANA H ASH, Manager,
New England Telephone
and Telegraph Company

Haverhill, Massachusetts

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor In addition to the articles enumerated in our letter of September 15 the following have been accepted:

Abbott Laboratories

Alternaria spp, Fungus Extract 5 per cent—Abbott
Aspergillus fumigatus, Fungus Extract 5 per cent—Abbott
Aspergillus niger Group, Fungus Extract 5 per cent—Abbott
Cephalothecium roseum, Fungus Extract 5 per cent—Abbott
Hormodendrum spp, Fungus Extract 5 per cent—Abbott
Monilia sitophila, Fungus Extract 5 per cent—Abbott
Mucor spp, Fungus Extract 5 per cent—Abbott
Penicillium rubrum, Fungus Extract 5 per cent—Abbott
Ustilago zeae (corn smut), Fungus Extract 5 per cent—Abbott
Yeast, Fungus Extract 5 per cent—Abbott
Tablets Barbitol—Abbott, 5 gr

Armour Laboratories

Gastric Mucin—Armour
Gastric Mucin Powder—Armour
Gastric Mucin Granules—Armour

Baxter Laboratories

Sodium Citrate 2½ per cent in Physiological Sodium Chloride Solution in the Transfuso Vac at Donor Set

Gilliland Laboratories

Typhoid-Paratyphoid Bacterial Vaccine, Immunizing, 50 cc vial

International Vitamin Corp

I V C Cod Liver Oil

Lederle Laboratories, Inc.

Capsules Sulfapyridine—Lederle, 0.25 gm

National Drug Co

Immune Globulin (Human) 2 cc. ampule vial
Immune Globulin (Human) 10 cc. ampule vial

Smith-Dorsey Co, Inc.

Tablets Sulfanilamide, 5 gr

E. R. Squibb & Sons

Ascorbic Acid—Squibb
Tablets Ascorbic Acid—Squibb, 25 mg

Tablets Ascorbic Acid—Squibb, 50 mg.

erick Stearns & Co

Gastric Mucin—Stearns

Gastric Mucin Powders—Stearns

Gastric Mucin Granules—Stearns

lac & Tiernan Products, Inc.

Azochloramud Saline Mixture 1 3300 Tablets, 85 gr

Wilson Laboratories

Gastric Mucin—Wilson

Gastric Mucin Powder—Wilson

Gastric Mucin Granules—Wilson

throp Chemical Co., Inc.

Fuadin

Ampules Solution Fuadin, 35 cc.

Ampules Solution Fuadin 5 cc.

PAUL NICHOLAS LEECH *Secretary*

North Dearborn Street,

Chicago, Illinois.

PORT OF MEETING

UR COUNTY MEDICAL SOCIETY

The annual meeting of the Four County Medical Society comprising the Berkshire, Franklin Hampden and Hampshire district medical societies, was held at Springfield, on Tuesday October 10. The subject under discussion was "Pain Its significance in diagnosis and prognosis." This was discussed from the viewpoint of general medicine by Dr Lewis M. Hurxthal Boston from that of general surgery by Dr Arthur W. Allen Boston from that of gynecology by Dr Joe V. Meigs Boston and from that of neurology by Dr Foster Kennedy professor clinical neurology Cornell University Medical School New York City.

Following the meeting a luncheon in honor of Dr Walter G. Pluppen president of the Massachusetts Medical Society was held at the Hotel Stonehaven with approximately 100 members attending. During the luncheon the following list of officers was submitted and elected for the ensuing year: president, Dr George L. Schadt, Springfield secretary, Dr W. Fenn Hoyt, Springfield vice-presidents, Dr Hugh J. Downey Pittsfield Dr Frederick J. Barnard, Greenfield, Dr John M. Murphy Florence, and Dr Frederic Hagler Springfield. It was voted to hold the next annual meeting at Greenfield.

NOTICES

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday November 22, from 2 to 4 p.m. Drs. Elliott C. Cutler and Soma will speak on "Headache." A clinicopathological conference, conducted by Dr Elliott C. Cutler will take place from 4 to 5 p.m.

On Thursday November 23 from 8:30 to 9:30 a.m. there will be at the Children's Hospital a combined clinic, conducted by Dr Kenneth D. Blackfan, of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER *M.D. Secretary*

BOSTON CITY HOSPITAL

The next clinical meeting of the Boston City Hospital will be held in the Cheever Amphitheater Thursday November 23, at 11:30 a.m. The subject "Water Metabolism" will be discussed in the manner of "Information Please."

Meetings are planned to be held in the Cheever Amphitheater the last Thursday of every month from November to May excepting December.

H. K. THOMPSON *M.D., Chairman*
Committee on Hospital Clinics.

BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club at the Boston Medical Library 8 Fenway Boston on Monday evening November 20 at 8:15. Professor Richard H. Shryock professor of American history University of Pennsylvania, will talk on "The Historian Looks at Medicine."

All those interested in the subject are cordially invited to attend.

PAUL D. WHITE, *M.D., President*
BENJAMIN SPECTOR, *M.D. Secretary*

BOSTON LYING IN HOSPITAL

Dr A. Louis Dippel will speak on "Visualization of Placenta in Utero" at the Boston Lying-in Hospital on Tuesday evening November 28 at 8:15.

Members of the medical profession are cordially invited to attend.

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide, former concert master with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra every

Thursday at 8:30 p.m., in Studio A, Station WMEX 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr Julius Loman Pelham Hall Hotel Brookline (BEA 2430).

BETH ISRAEL HOSPITAL

Professor Bernhard Zondek will lecture on "Inhibition of the Anterior Pituitary Function Through the Estrogenic Hormone" with illustrated lantern slides at the auditorium of the Beth Israel Hospital on Saturday morning November 18 at 10:30.

Physicians and medical students are cordially invited to attend.

UNIVERSITY EXTENSION COURSES

A university extension course on "Practical X-Ray" designed for technicians nurses, medical secretaries and others who need to know more about the subject is to be given by the Massachusetts Department of Education on Thursday evenings at 7:45 o'clock in Harvard Hall, Harvard University. The first meeting of the class will be on November 23.

The class will be led by Max Ritvo, *M.D., instructor in*

roentgenology, Harvard Medical School The lectures will cover the history and theory of x rays and the design and operation of different x-ray machines and tubes Applications to medicine, science, industry and the arts will be discussed and illustrated extensively by films and lantern slides X-ray and radium treatment of diseases also will be touched on briefly

MASSACHUSETTS HOSPITAL ASSOCIATION

The third mid year dinner meeting of the Massachusetts Hospital Association will be held at the Parker House, Boston, on Tuesday, December 5, at 6 30 p m

MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS

There will be a meeting and dinner of the Massachusetts Society of Examining Physicians at the Copley-Plaza Hotel on Wednesday evening, November 22, at 6 30 Dinner will be \$2 50 per plate.

PROGRAM

Narcotics Assistant United States Attorney William T McCarthy, in charge of the Criminal Division
The Cause and Manner of the Squalus Deaths Dr William J Brickley

MATTHEW V NORTON, M.D., *President*,
WILLIAM P COUES, M.D., *Secretary*

WACHUSETT MEDICAL IMPROVEMENT SOCIETY

A meeting of the society will be held at Holden District Hospital on Wednesday, December 6, at 6 30 p m Dr John Dumphy, of Worcester, will speak on "Sulfanilamide, Sulfapyridine and Related Compounds"

Members of the profession are cordially invited to attend

LEROY E MAYO, M.D., *Secretary*

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held at the Massachusetts General Hospital, on Monday, November 27, at 8 15 p m

PROGRAM

Demonstration of Specimens Dr Paul D White.
Non luteic aortic aneurysms dissecting aneurysm of the aorta followed a year and a half later by a new dissecting aneurysm of the aorta with rupture and death

Arteriosclerotic thoracic aortic aneurysm with rupture.

Healed subacute bacterial endocarditis in a heart showing active rheumatic myocardial involvement.

Variations in PR Interval and Duration of the QRS Waves in the Classic Leads The possibility of error in the measurements Drs P D White, C E. Leach and S A Foote.

Demonstration of Lag Screen for Visualization of Electrocardiogram (Cardioscope) Dr H B Sprague.

The Clinical Significance of Low Voltage of the QRS Waves in the Classic Leads and Lead 4 Drs C E. Leach and P D White

An Autopsy Study of the Relations of Gall Bladder Disease and of Peptic Ulcer to Coronary Disease Drs B J Walsh, E F Bland and P D White.

A Note on Vagotonia and Coronary Disease Dr Alberto Taquini

Subacute Bacterial Endocarditis Drs S Kelson and P D White.

Analysis of 250 cases from 1924 to 1938 inclusive with particular reference to diagnosis and prognosis

New therapy sulfapyridine and heparin combined
Cervicothoracic Sympathectomy in Preference to Paravertebral Alcohol Injection for Angina Pectoris with High Radiation of Pain New technique Drs J C White and H B Sprague.

Interested physicians and medical students are cordially invited to attend

EDWARD F BLAND, M.D., *Secretary*

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The written examination and review of case history (Part I) for Group B candidates will be held in the various cities of the United States and Canada on Saturday January 6, 1940, at 2 00 p m Formal notice of the place of examination will be sent each candidate several weeks in advance of the examination date No candidate will be admitted to examination whose examination fee has not been paid at the secretary's office. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held in June, 1940 Receipt of Group B applications for the current examination (January 6, 1940) closed October 4

Candidates who are required to take re-examination must do so before the expiration of three years from the date of their original examination.

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire board, meeting in Atlantic City, New Jersey on June 8, 9, 10 and 11, 1940, immediately prior to the annual meeting of the American Medical Association in New York City

Application for admission to Group A, Part II, examinations must be on file in the secretary's office not later than March 15, 1940

After January 1, 1942, there will be only one classification of candidates, and all will be required to take the Part I and Part II examinations For further information and application blanks, address Dr Paul Titus, secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, NOVEMBER 20

MONDAY NOVEMBER 20

- *11 30 a m Carney Hospital Monthly clinical meeting and luncheon.
- *12 15 p m -1 15 p m Clinicopathological conference. Dr S. F. Wolbach Peter Bent Brigham Hospital amphitheater
- *8 15 p m Boston Medical History Club Boston Medical Library 8 Fenway Boston

TUESDAY NOVEMBER 21

- *9 10 a m Personality of the Criminal Dr A Warren Sears Joseph H Pratt Diagnostic Hospital
- *10 a m -12:30 p m Boston Dispensary tumor clinic
- *12 m South End Medical Club Headquarters of the Boston Tuberculosis Association 554 Columbus Avenue Boston

11.15 p.m.-11.15 p.m. X-ray conference Dr Merrill C. Sosman.
Peter Bent Brigham Hospital amphitheater

THURSDAY NOVEMBER 22

9-10 a.m. Hospital case presentation. Dr S J Thannhauser
Joseph H Pratt Diagnostic Hospital

11 a.m. Clinicopathological conference. Children's Hospital amphitheater

1 p.m.-4 p.m. Joint medical and surgical clinic Peter Bent Brigham Hospital

6.30 p.m. Massachusetts Society of Examining Physicians. Copley Plaza Hotel Boston.

FRIDAY NOVEMBER 23

8.30 a.m.-9.30 a.m. Combined clinic of the medical surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital, at the Children's Hospital

9-10 a.m. Diabetic Clinic. Dr Joseph Rosenthal Joseph H Pratt Diagnostic Hospital.

11.30 a.m. Boston City Hospital Clinical meeting

SATURDAY NOVEMBER 24

9-10 a.m. Clinicopathological conference Dr Soma Weiss and Dr Rudolf Osmond. Joseph H. Pratt Diagnostic Hospital

10 a.m. 11.30 p.m. Boston Dispensary tumor clinic.

SUNDAY NOVEMBER 25

9-10 a.m. Hospital case presentation. Dr S J Thannhauser Joseph H. Pratt Diagnostic Hospital

10 a.m.-12 m. Medical staff round of the Peter Bent Brigham Hospital. Conducted by Dr Soma Weiss.

*Open to the medical profession.

NOVEMBER 17—Boston Lying In Hospital. Page 758, issue of November 9

NOVEMBER 18—Beth Israel Hospital Boston. Page 79

NOVEMBER 20—Corney Hospital. Monthly clinical meeting and lecture. Page 79 issue of November 9

NOVEMBER 20—Boston Medical Library Club. Page 797

NOVEMBER 21—South End Medical Club. Page 799 issue of November 9

NOVEMBER 21—Lawrence Cancer Clinic. Page 759 issue of November 9

NOVEMBER 22—Peter Bent Brigham Hospital. Joint medical and surgical clinic. Page 797

NOVEMBER 22—Massachusetts Society of Examining Physicians. Page 798

NOVEMBER 23—Combined clinic of the medical surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital. Page 79

NOVEMBER 23—Boston City Hospital. Clinical meeting. Page 797

NOVEMBER 24—Boston Dispensary. Luncheon meeting and the clinical staff. Page 754 issue of November 9

NOVEMBER 25—Joseph H Pratt Diagnostic Hospital. Page 798 issue of November 9

NOVEMBER 27—New England Heart Association. Page 798

NOVEMBER 28—Boston Lying In Hospital. Page 797

DECEMBER 2—American Board of Obstetrics and Gynecology. Page 1019 issue of June 15.

DECEMBER 5—Massachusetts Hospital Association. Page 798.

DECEMBER 6—Wachusett Medical Improvement Society. Page 798

DECEMBER 6—New England Obstetrical and Gynecological Society. Page 79 issue of November 9

DECEMBER 8—William Harvey Society. Page 676, issue of October 26.

DECEMBER 13—Fenwick Association of Physicians. 8.30 p.m., Hotel Fenwick, Fenwick.

JANUARY 6, [Jan 8-11 1940]—American Board of Obstetrics and Gynecology. P 1019, issue of July 27 and page 798

JANUARY 22-25 1940—American Academy of Orthopaedic Surgeons. Hotel Statler Boston.

FEBRUARY 11-14—International College of Surgeons. Page 759 issue of November 9

MARCH 2, [Jan 8 and 10]—American Board of Ophthalmology. Page 719 issue of November 2.

MARCH 7-9 1940—The New England Hospital Association. Hotel Statler Boston.

MAY 14 1940—Pharmacopoeial Convention. Page 804 issue of May 25.

JUNE 7-9 1940—American Board of Obstetrics and Gynecology. Page 1019 issue of June 15.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 3, 1940—Semi-annual meeting. Combined meeting with Essex South. Dravers State Hospital, Hathorne. 7 p.m.

ESSEX SOUTH

DECEMBER 6—"Psychoneurosis and its Relation to Other Inflammatory Diseases of the Kidney." Dr Soma Weiss. Salem Hospital, Salem.

JANUARY 3 1940—"Head Injuries. Dr John S. Hodgson. Dravers State Hospital, Hathorne.

FEBRUARY 14—"Cough, Sputum, Hemoptysis—How shall they be investigated? Dr Rere H. Berra. Essex & Haverhill, Haverhill.

MARCH 6—"Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections. Dr Champ Lyons. Lynn Hospital, Lynn.

APRIL 3—Addison Gilbert Hospital Gloucester

MAY 8—Annual meeting. Salem Country Club Peabody

HAMPSHIRE

JANUARY 10, 1940.

MARCH 13.

MAY 8.

All meetings are held at 11.30 a.m. at the Cooley Dickinson Hospital, Northampton.

MIDDLESEX EAST

JANUARY 10, 1940.

MARCH 20.

MAY 15.

Meetings are held at 12.15 p.m. at the Uxton Country Club, Stokenham.

PLYMOUTH

JANUARY 18 1940—Brockton Hospital, Brockton.

MARCH 21—Goddard Hospital Brockton.

APRIL 18—State Farm.

MAY 16—Lakeville Sanatorium, Lakeville.

SUFFOLK

NOVEMBER 29—Scientific meeting. Treatment of Syphilis. Dr Harold T. Hyatt. Dr Louis Chargin, and Dr William Lever of New York City

JANUARY 21—Scientific meeting. Symposium on Ulcerative Colitis and Diarrhea. Under the direction of Dr Chester M. Jones.

APRIL 24—Annual meeting in conjunction with the Boston Medical Library. Election of officers. Program and speakers to be announced later

JUNE 27—Scientific meeting. Symposium on Ulcerative Colitis and Diarrhea. Under the direction of Dr Chester M. Jones.

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BOOKS RECEIVED FOR REVIEW

Nursing Mental Diseases Harriet Bailey. Fourth edition. 264 pp. New York The Macmillan Co., 1939 \$2.50

Infections of the Hand Lionel R. Fifield. Second edition by Patrick Clarkson. 167 pp. New York Paul B. Hoeber Inc., 1939 \$3.25

A Textbook of Pathology for Nurses Coleman B. Rabin. Second edition, revised. 260 pp. Philadelphia and London W. B. Saunders Co., 1939 \$1.75

An Introduction to Genetics A. H. Sturtevant and G. W. Beadle. 391 pp. Philadelphia and London W. B. Saunders Co., 1939 \$3.25

Laboratory Manual for Animal Histology Clair A. Hannum. Third edition. 105 pp. Tucson University of Arizona 1939 \$1.75

Injuries of the Nervous System Including poisonings Otto Marburg and Max Helfand. 213 pp. New York. Veritas Press 1939 \$3.00

BOOK REVIEWS

Clinical Studies in Psychopathology. A contribution to the etiology of neurotic illness Henry V. Dicks. 248 pp. Baltimore William Wood & Co., 1940 \$4.75

The material of this volume originally formed a series of postgraduate lectures given at the Tavistock Clinic as part of a larger course in psychotherapy. According to the author the subject matter necessitated an acquaintance with the major modern schools of psychotherapy; therefore, it lays no claim to originality, and merely represents the contribution of one individual to current discussions of the psychoneuroses. It is based on the contributions of Freud and of those who, according to the author have extended Freud's teachings (Jung and Adler)

The volume discusses, in turn, anxiety and obsessional states, hysteria, ambivalence, drug addictions, sexual perversions and inversions and abnormalities in sexual function. The author omits any detailed discussions of such important psychopathological states as reactive depressions, character disorders and organ neuroses, although in the last chapter he gives an outline of his general ideas on these subjects.

The theoretical part of the book is illustrated by sixty-two clinical histories, and by means of this material, he formulates three main instinctive tendencies—the self-preservative, the sexual (Freud's libido concept) and the aggressive. It appears to the reviewer that this formulation of the instincts is too artificial, as no instinctive drive ever appears in pure culture, but is admixed, frequently overlaps and is subject to complicated vicissitudes.

The author is an eclectic, although on every major point he is in agreement with the dynamic formulations of Freud. He emphasizes that in psychoanalytic therapy we have a weapon of attack on the neuroses which answers to the requirements of science. However, in order to shorten the psychotherapeutic procedures, he tends to direct the free associations by attempting to keep the associations to a stimulus idea, namely the most important symptom. This technical procedure somewhat resembles the obtaining of an associative anamnesis. In conclusion he states what psychoanalysis has emphasized almost from its beginnings—that analytic treatment is directed not only to a removal of symptoms, but also to an altering of the personality in the direction of social and psychologic maturity.

Public Health Law James A. Tobey. Second edition. 414 pp. New York: The Commonwealth Fund, 1939. \$3.50.

This second edition deals with much of historical and evolutionary interest in the development of our present-day public-health laws. The material contained is of primary importance to public health administrators, and none should dabble in legislative matters pertaining to public health without some such guide to reliable and authoritative sources of legal information. Something over two thousand cases are referred to and indexed. Some general principles are enunciated, for example, laws should be enacted for enforcement only, never for educational purposes. It is of interest to note that Congress created a National Board of Health in 1879. It died because it was not, as we now say, adequately implemented. Altogether the book is a very worthwhile compilation.

Les Occlusions Artérielles Aigues des Membres Formes cliniques, indications physiopathologiques et thérapeutiques H. Hamovici. 124 pp. Paris: Masson et Cie, 1939. 26 Fr. fr.

This is a stimulating little book on all phases of acute occlusions of the peripheral arteries including both thrombosis and embolism and touching on other causes that are uncommon. Because the material is almost entirely clinical, the practitioner will find this book handy for quick reference.

The author emphasizes the role of vasomotor spasm in acute occlusions and suggests the relief of this spasm by medication or sympathetic attack before the performance of embolectomy. Obviously influenced by Leriche, he moreover advises the excision of the thrombosed artery,

regardless of whether the process be primary, or secondary to an embolus. He attempts no evaluation of pressure therapy in these conditions.

The author comes from a group of men who promoted our knowledge of the interrelation of the arteries and the veins, and one therefore finds a pertinent discussion of the venous complications of arterial involvement.

The absence of plates and the lack of a good bibliography are somewhat disappointing.

The Hair and Scalp. A clinical study Agnes Savill. Second edition. 309 pp. Baltimore: William Wood Co., 1937. \$4.75.

This book is an amplification and revision of the first edition, but the general arrangement remains the same. In that diseases are considered according to symptoms rather than etiology. The latter makes easy identification of the particular scalp trouble at hand for those untrained in dermatology.

After a chapter on the structure and physiology of hair, gray hair is taken up, with advice not to dye, although in a later chapter the subject of dyeing is extensively discussed and its disadvantages pointed out. The author advises extensive brushing and combing of hair, disposes of the superstition that cutting a woman's hair short stimulates its growth, and shows by microscopic study that singeing is somewhat harmful. She very sensibly advises washing the hair when it needs it rather than by any set schedule of weeks; she shows that so at least at times, may need to wash the hair every day and without any harm whatever so long as it is carefully done and properly dried, whereas other scalps remain clean in regions of clear atmosphere that they may need washing for months.

The book is written for the general practitioner, who will find many helpful points. Although the dermatologist might prefer a more scientific arrangement, he will find the book very useful.

Epidemic Encephalitis. Etiology, epidemiology, treatment Third report by the Matheson Commission. 493 pp. New York: Columbia University Press, 1939. \$3.00.

The Matheson Commission for the Study of Epidemic Encephalitis, established in 1927, has published two previous reports on the subject (1929 and 1932). Both of these proved invaluable to investigators, as well as to public health officials. In the last seven years, much new material has been published in regard to epidemic encephalitis, in spite of the fact that the disease has not appeared in epidemic form during this period.

The third report covers the entire literature from 1930 to 1937. The work, moreover, done on the viruses that have been isolated in relation to epidemic encephalitis, on varied allied diseases and on vaccines is clearly outlined in preliminary chapters. The most important additions are those relating to human encephalitis caused by the viruses of Eastern and Western equine encephalitis, post-vaccinal encephalitis, postinfectious encephalitis, hemorrhagic encephalitis and various related diseases, such as lymphocytic choriomeningitis.

The book is adequately indexed and published in a convenient size and format. It is one that no worker in the field of virus diseases can possibly afford to be without.

The New England Journal of Medicine

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NOVEMBER 23, 1939

NUMBER 21

MASSACHUSETTS MEDICAL SOCIETY

Section of Radiology and Physiotherapy

RADIOTHERAPY FOR INFLAMMATORY CONDITIONS*

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The treatment of inflammatory processes with roentgen rays is far from new. Indeed it dates back to about 1900. The earliest mention of the subject is to be found in papers by Freund¹ and Schönberg,² Gautier,³ Rudis Jicinsky⁴ and "and in the books of Williams"⁵ and Belot.⁶ An interesting point is that some of the earliest cutaneous trials were made in this country but received no attention until the successful results had been repeatedly confirmed by others abroad.

Many physicians are unaware of the favorable results of roentgen rays or radium on various types of acute or chronic inflammation. Yet the cutaneous value of irradiation in inflammations has been thoroughly substantiated, and the testimony is so generally favorable that one wonders why it is not used more than it is or why, in many cases, it is employed only after other therapeutic measures have failed to yield the desired results. Perhaps the very multiplicity of inflammatory lesions for which radiotherapy has been claimed to be effective has led to a natural skepticism. Also, the many explanations which have been advanced to account for the favorable results of roentgen rays or radium on inflammation have probably led many physicians to doubt the evidence or to ascribe the favorable results to enthusiasm or to psychic factors. Indeed, without a convincing explanation it would be difficult to believe that the same agent could be so therapeutically effective against so many different types of inflammation. And yet the reason appears to be simple and to rest on abundant experimental evidence.

Others who have heard or read of the therapeutic possibilities of irradiation in inflammatory processes hesitate to make use of the method because they fear deleterious effects on the skin or gastrointestinal disturbances such as are observed in connection with the treatment of malignant tumors. When treating neoplasms the aim is to deliver the largest dose compatible with the integrity of the surrounding tissues. When treating inflammatory lesions, on the contrary, only small or moderate doses are employed. Doses that might strain the tolerance of the skin are unnecessary and should be avoided as potentially dangerous. For acute inflammations especially, the doses required are so small that the skin or the gastrointestinal tract cannot possibly be affected. Hence any fear on this score is unfounded.

ACUTE INFLAMMATIONS

Many varieties of acute inflammation yield rapidly to a small dose of roentgen rays. By a small dose is meant one representing less than half the tolerance dose of the skin—a dose as small as a fourth of the so-called erythema dose or even less, is often sufficient, but this may vary somewhat according to the character and stage of the lesion in a given case. A significant point is that the more acute the inflammation, the smaller the dose of rays required. With such small doses there can be no question of cutaneous or systemic reaction; therefore weak and febrile patients can be treated without danger. In most cases a single exposure is sufficient but occasionally it may be advisable to repeat the treatment a few days later. This is particularly true when the initial dose has been exceptionally small or when the region treated has not been wide enough.

Among the acute inflammatory conditions in which the therapeutic value of irradiation has been

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established are furuncle, carbuncle, abscess, cellulitis and phlegmon, onychia and paronychia, acute adenitis, pneumonia, acute parotitis and erysipelas. In other forms of acute inflammation, such as sinusitis, otitis and mastoiditis, pelvic infection, osteomyelitis and gas-bacillus infection, a considerable body of evidence indicates an equally favorable response in many cases, but more controlled evidence will be required to be convincing.

Pyogenic Infection When irradiated early, during the stage of maximal leukocytic infiltration, many lesions due to pyogenic cocci do not suppurate, their evolution is arrested and they undergo spontaneous resolution. Therefore the treatment is most effective when other methods of treatment are least effective, it is painless, and does not interfere with the activities of the patient. Pain is often relieved in a few hours, but sometimes the relief may be preceded by exacerbation for a brief period. Hot or other dressings are often unnecessary, or the period during which they must be applied is shortened. Treatment after suppuration has set in tends to hasten the suppurative process, the duration of which may thus be more or less diminished. Hence the patients should be kept under close observation so that, if necessary, the surgeon may provide adequate drainage at the proper time. But acute pyogenic inflammations do not always respond so favorably, in a minor proportion of cases they yield little or not at all. This is especially true when the treatment is started long after the onset, that is, late in the course of the inflammation, when exudates have undergone organization and when some degree of connective-tissue proliferation has occurred.

Pneumonia As early as 1905 and 1906, Musser and Edsall³⁴ and Edsall and Pemberton⁶ observed and reported the strikingly favorable influence of a small dose of roentgen rays in 4 cases of delayed resolution of lobar pneumonia. Every other therapeutic measure having failed to improve the pulmonary condition of the patients, roentgen irradiation was tried as a last resort. Within twenty-four hours after exposure, resolution of the pneumonic exudate set in and proceeded rapidly, and the patients recovered. These observations were subsequently confirmed by Quimby and Quimby,³⁶ Krost³¹ and Torrey.⁴¹ In fact, the Quimbys were so impressed by the rapid influence of irradiation in 10 cases that they were impelled to testify that "no pathologic process in the body responds quicker to an x-ray exposure than the non-resolution following pneumonia." Since then Heidenhain and Fried,⁴³ Holzknecht,³⁹ Merritt and McPeak³³ and others have observed favorable action of roentgen rays on postoperative pneumonia, as well

as on pneumonia unrelated to surgical intervention, in a large percentage of cases in which the treatment was employed. Naturally, the best results are to be obtained from early treatment. As pointed out by Musser and Edsall, irradiation cannot be expected to have much effect once the pneumonic inflammation has become organized or when the treatment is given shortly before impending death.

Acute Parotitis Every surgeon is aware of the sinister character of that form of acute parotitis which arises as a complication of certain operations, especially those on the large intestine, and of the high mortality associated with it. The first record of the favorable effect of irradiation on this disease appears to have been made by Heidenhain,²² who found that the inflammation reacted much as do other acute inflammatory processes. Rankin and Palmer³⁷ found that a moderate dose of radium, applied soon after the onset, caused the inflammation to subside in most cases within twenty-four to forty-eight hours. Moreover, suppuration usually did not occur, and the mortality was correspondingly reduced. Radium is sometimes preferable because the treatment can thus be given without disturbing the patient. When portable roentgen therapeutic apparatus is available, however, this is an advantage because the necessary dose can be given in much less time than with radium.

Erysipelas When erysipelas does not complicate diabetes or nephritis, roentgen irradiation is usually followed by prompt abatement of the fever and recession of the lesions. This is especially true when the patients are adults and when the treatment is given early. In children, for some unknown reason, the disease does not respond quite so well. In some cases, after an initial period of improvement, the inflammation may again become active, and additional treatment may be required to arrest the process. When this happens, it is usually because the initial treatment was confined too closely to the apparent limits of visible involvement. Too much stress cannot be laid on the importance of including in the field of irradiation a wide zone of apparently normal tissue around the lesion. A single dose, corresponding to 100 or 200 r, generated at 130 or 140 kilovolts and filtered through 4 mm of aluminum, is usually sufficient.

Favorable results may also be obtained by exposing the affected region to an erythema or blistering dose of ultra-violet rays. A possible disadvantage is that during the period of cutaneous reaction to treatment it may be difficult to know what is disease and what represents reaction. Roentgen irradiation has no such disadvantage, the dose required does not cause reactive inflammation.

Other Acute Inflammations Other acute inflammations have been found to yield equally well to roentgen irradiation. Some years ago Granger¹⁰ reported that in certain cases of acute mastoiditis in which the mastoid region had been exposed to small doses of roentgen rays for diagnostic purposes the inflammation had subsided and an operation had been unnecessary. Similar reports have appeared since then, but some of these have been rather too casual to be convincing. I am not aware that the possible therapeutic advantage of irradiation in this condition has ever been given a serious and thorough test. This is unfortunate, because if acute mastoiditis should be found to yield as do so many other forms of inflammation, many patients might be saved some of the painful stress and cost of hospitalization associated with operations for the condition. Moreover, this possibility could be tested without jeopardizing the interests of the patients in any way.

In 1936, Kelly and Dowell²¹ reported that favorable results had been obtained in cases of gas bacillus infection. Since then, these authors have published several additional reports based on a larger number of cases. According to them, the only patients who died were those in whom an affected extremity had been amputated. The number of cases included in their latest report² is now sufficient to command attention, especially since they appear to have succeeded in reducing the mortality to less than 10 per cent when amputations were necessary, and to less than 5 per cent when they were not. If the experience of others should confirm the results obtained by Kelly and Dowell, roentgen therapy might be shown to be a great boon to patients afflicted with this virulent form of infection.

In treating inflammations caused by such virulent bacteria Kelly and Dowell have found it advantageous to use doses as small as 100 r and to repeat them daily or twice daily for three or four days. Although the reason why this procedure is more effective is not clear, it is possible that when the infecting bacteria have a high degree of virulence a single irradiation does not influence a sufficient number of circulating leukocytes to overcome the infection. But when irradiation is repeated daily or twice a day for three or four days, the number of leukocytes acted on by the rays must necessarily be much greater, and this may account for the greater efficacy of this method in the treatment of gas-bacillus infection. Inasmuch as streptococcal infections often assume a virulent form and leukocytic infiltration is often slight or wholly lacking, it is possible that the same method of small doses repeated daily or twice daily for

three or four days would have a similar advantage.

Type of Rays The quality of the rays is of secondary importance. Favorable results may be obtained with rays generated at 100, 140 or 200 kilovolts. If in most cases the results obtained with rays generated at 130 or 140 kilovolts seem superior to those obtained with rays generated at a higher potential, this is almost certainly not due to any specific action of rays of different wave length, but probably to a difference in absorption by the inflamed tissues. A larger proportion of rays of medium wave length than of rays of short wave length is absorbed in the first few centimeters of tissue. Therefore, since the majority of the inflammatory conditions mentioned are near the surface, the advantage, so far as maximal absorption at the desired level is concerned, would seem to favor rays of medium wave length. When the inflammation is deep in the chest, rays of short wave length might be preferable. However, since the most effective dose is small this theoretical advantage is not an important factor.

CHRONIC INFLAMMATIONS

For years it has been known that many forms of chronic inflammation are favorably influenced by roentgen irradiation. Among these may be mentioned numerous varieties of chronic inflammation of the skin in which the therapeutic value of radiotherapy is conceded by experienced dermatologists. Other chronic inflammatory processes which may be cited are tuberculous adenitis, peritonitis, keratitis and iritis, actinomycosis and blastomycosis, trachoma in its early stages and active infectious arthritis. Two features which characterize this type of irradiation are that the dose of roentgen rays must be larger than that used for acute inflammations and that treatment must be repeated at intervals for some time. By a larger dose is meant a dose varying between 50 and 80 per cent of the tolerance dose when given at one time or in international units, between 300 and 500 r according to the conditions of irradiation. Rays generated at 120 or 140 kilovolts and filtered through 4 or 6 mm of aluminum are usually adequate. Rays generated at higher potentials can be used with approximately equal effect. For skin diseases, unfiltered rays or rays filtered through 2 mm of aluminum and generated at 80 or 100 kilovolts are generally preferable. The treatment of chronic inflammatory lesions with maximal (erythema, tolerance or tumor) doses is bad practice and should be avoided as potentially dangerous. Since treatment must be repeated at intervals for varying periods, the use of maximal doses may lead to undesirable effects or, by superimposing a

reactive inflammation, may cause the original inflammation to spread rather than to abate

Tuberculous Processes Although considerable variation may be observed in different cases, the effect of irradiation on tuberculous processes is characteristically slow. In tuberculous adenitis the affected region must be irradiated every three or four weeks for three to twelve months. When calcification is absent, the inflamed nodes gradually recede and may disappear completely, or may remain as small fibrous granules. Unless abundant, caseous material may be absorbed or may be replaced by calcium. When suppuration occurs drainage may be advisable, but sometimes the pus can be withdrawn through a needle of large bore, which should be introduced not through the thinnest part of the fluctuant region, but to one side through more substantial tissue, so as to avoid the formation of a sinus. The extensive surgical procedures formerly in vogue are now seldom necessary. The resolution of tuberculous lesions appears to be hastened by supplementing periodic roentgen irradiation with daily exposure of the entire body to graduated doses of sunlight or to ultra-violet rays generated artificially. Ultra-violet irradiation confined to the affected region is usually a waste of time.

Much the same may be said of tuberculous peritonitis. An important consideration is that the entire abdominal cavity should be irradiated as uniformly as possible. This can best be done by dividing the anterior half of the abdomen from the level of the diaphragm to that of the pubic region into four fields, with the navel as the common center, the posterior half should be divided into four corresponding fields.

Radiotherapy is also an effective method of treating tuberculosis of the corner or iris. The lesions recede more rapidly after exposure to roentgen rays than do similar lesions in other parts of the body. The dose of roentgen rays should never exceed three fourths of a minimal erythema dose, a larger dose, especially in children, may lead to epithelial degeneration of the crystalline lens and to cataract formation.

Actinomycosis When actinomycosis affects the face, mouth or other superficial structures, roentgen or radium irradiation, supplemented by the internal use of large doses of iodides and sometimes by simple surgical drainage of an abscess, is the most effective therapeutic measure, and a large proportion of patients can thus be permanently cured.

Not infrequently actinomycotic inflammation arises in the intestine especially the lower part of the small intestine, where it is often mistaken

for simple or suppurative appendicitis. In many cases one or more operations are performed, and the true character of the process is not recognized. This is unfortunate because, if the lesion is actinomycotic in character, exploratory maneuvers or any measures beyond simple drainage of an abscess serve only to spread the infection. Thorough exposure of the entire abdomen (front and back) to about three fourths of an erythema dose of roentgen rays, repeated every three or four weeks, may be followed by substantial improvement and sometimes by complete and permanent cure. But when the infection has extended to the respiratory tract (bronchi, lungs and pleura), more than slight and temporary improvement is not likely to be obtained with any method of treatment.

Trachoma Trachoma is characterized by conjunctival granulations composed largely of lymphocytes. These granulations are gradually replaced by connective tissue, and the eyelids become sclerosed and distorted. As early as 1902 and 1903, Mayou³⁰ and Stephenson and Walsh³¹ and Cassidy and Rayne⁴ made the discovery that, in some cases, the trachomatous granulations receded after exposure to roentgen rays, and that the patients were cured. Subsequently, Thielemann,⁴ Cochard⁶ and Meldolesi and Sabbadini³² confirmed the favorable influence of radiotherapy. Sometimes the lesions recurred later, but resumption of treatment caused them to retrogress and disappear, this probably meant that the initial treatment had not been continued long enough. The evidence furnished by the group of writers last mentioned indicates that the action of the rays is greatest during the early stages of the ulcer form of the disease and least during the late stages, when the granulations have been replaced by connective tissue.

Chronic Infectious Arthritis In many cases roentgen irradiation relieves pain and reduces swelling, and the functional disability diminishes. As might be expected, the degree of improvement varies considerably in different patients. The best results require repeated treatment and are obtained in cases in which the inflammation is active. Incidentally, a useful indication of active inflammation is tenderness. When the inflammatory deposits have become largely or completely organized, little improvement is to be expected. Of course, focal infection must not be neglected, irrespective of irradiation.

Bronchiectasis Recently Berck and Harris³ reported having treated with roentgen rays 30 patients with bronchiectasis, of whom 19 are said to have derived more or less pronounced improve-

ment. Here again an opinion about the value of irradiation will have to await corroborative testimony. However, the care with which the cases appear to have been selected and the degree of improvement obtained in many of them make this report seem worthy of attention.

GENERAL

One consideration cannot be stressed too much and the inability of some radiologists to obtain satisfactory results is often due to their failure to realize its importance. This consideration is that, in chronic inflammations generally treatment must be continued for a long time. Even after the lesions and symptoms have disappeared or have ceased to be active, it is wise to treat the patient once or twice more. The more chronic the lesion the more essential is this precaution. As examples I need only cite tuberculous adenitis, peritonitis, arthritis and synovitis. The response of tuberculous lesions to roentgen irradiation varies considerably from one patient to another but in general it is characteristically slow. When treatment is stopped too soon, what might have been an excellent and permanent result is spoiled after a period of apparent arrest, the tuberculous process becomes active again, and resumption of treatment may not be so effective as before. Greater persistence in the first instance is usually the best policy.

When dealing with acute or chronic inflammatory lesions, a most important point is that the concept of maximal, tolerance or tumor doses must be abandoned. Not only are they less effective than they are actually dangerous. To employ such doses in treating inflammatory conditions constitutes a loss of electrical energy, a gross waste of time on the part of the personnel as well as that of the patient and an unwarranted increase in cost. But, still more important, there is danger of inducing in the affected tissues an inflammatory reaction independent of that which is already present, and this might readily lead to spread rather than resolution of the infection. The principles of sound treatment are thus violated. This probably explains why some radiologists have failed to obtain the favorable results which should follow proper treatment. Furthermore the possibility of spreading the infection by excessive doses is not the only danger. Experiments on animals carried out by Lacassagne and Vincent²⁵⁻²⁹ have shown that, when acute inflammatory lesions are induced by injecting *Streptobacillus cariae* into rabbits were exposed to doses of roentgen rays such as are used in the treatment of malignant processes, in a considerable proportion of animals sarcomas subsequently developed in the same region.

MODE OF ACTION

Acute Inflammations Numerous experiments have long since made it clear that most bacteria are not directly influenced to a perceptible degree by doses of roentgen rays or radium such as are commonly employed in treating human beings. To attribute the favorable effect of irradiation to a bactericidal action of the rays, therefore, would be to maintain an untenable hypothesis. Certainly there is little ground for the assumption that irradiation increases the production of antibodies. On the contrary, the experiments of Hektoen¹⁷⁻¹⁹ and others indicate that irradiation tends to diminish the formation of antibodies. Nor does the evidence now available justify one in assuming that any difference in the quality of the rays has a direct effect on the result but the quality of the rays may and probably does have an indirect effect because it influences the proportion of rays absorbed at different depths beneath the surface.

Anyone who has had an extended experience with radiotherapy for acute inflammations cannot have failed to be impressed by the prompt relief of pain and the rapid resolution of the lesions when treated early, as well as by the acceleration of suppuration in lesions treated later, by the fact that acute inflammations of different kinds respond at about the same rate to a given dose when treated at a corresponding stage, and by the circumstance that a small dose of rays is sufficient to produce this effect. Since irradiation acts in the same way and within the same time on so many forms of acute inflammation, it seems logical to conclude that the lesions themselves must have some common factor. This factor appears to be the radiosensitivity of certain cells which are a more or less prominent feature of the majority of acute inflammations.

Pyogenic infections in general are characterized by varying degrees of leukocytic infiltration. By accumulating leukocytes, chiefly lymphocytes, polymorphonuclear cells and eosinophils around one or more clusters of bacteria, the body attempts to localize the infection, destroy the invading organisms and neutralize their toxic products. The leukocytic infiltration also appears to be Nature's method of intensifying the production of antibodies. An additional factor is hyperemia which facilitates the mobilization of leukocytes. Of some acute inflammations especially those caused by streptococcal infection, local infiltration by leukocytes is not a prominent feature. Against infections of this kind the body apparently defends itself by a general reaction of the leukocytes in the circulating blood.

Experiments on a large number of animals of different species and observations on human beings

is to the effect of roentgen rays and radium on different kinds of cells and tissues have proved conclusively that each variety of cell has a specific range of sensitiveness to irradiation. Some are extremely sensitive, even to small doses, while others are not influenced by doses many times larger. Moreover, these experimental and clinical investigations have demonstrated that the most sensitive of all cells are the lymphocytes in the spleen, lymph nodes, lymph follicles, thymus gland, circulating blood and bone marrow. The polymorphonuclear and eosinophilic leukocytes are also sensitive, but their susceptibility to irradiation is slightly less than that of the lymphocytes. When the entire body of an animal is exposed to a moderate dose of roentgen rays or radium, the majority of the organs remain free from perceptible abnormalities, but the spleen, lymph nodes and intestinal lymph follicles show a destruction of lymphocytes, the degree of which varies according to the dose of rays and the interval between irradiation and the removal of the tissue.

As observed by Heineke,¹⁴⁻¹⁶ the disintegration of lymphocytes was characterized by disorganization and fragmentation of the nuclear chromatin of the cells and by scattering of the fragments of chromatin between the remaining intact cells and in the spaces of the reticular stroma, where the fragments gathered into clumps or balls. The latter were gradually taken up by some of the reticular cells, which assumed a phagocytic property and swelled as the amount of ingested chromatin debris increased. This process was associated with a progressive reduction in volume of the affected lymphoid structures. Identical changes were observed in the lymphoid tissue of the vermiform appendix and in the bone marrow. The destruction of lymphocytes in the spleen and lymph nodes was often so great that most of the malpighian corpuscles or lymph follicles could be recognized only by the blood vessels and by the concentric arrangement of the stroma. A small percentage of lymphocytes appeared to resist the action of the rays. After a number of hours, the phagocytic reticular cells (macrophages) themselves began to disappear. The chromatin debris ingested by the phagocytes appeared to undergo intracellular digestion, because the number and size of the ingested fragments diminished steadily. Two or three days after irradiation, degenerative alteration of other cells, notably the polymorphonuclear leukocytes and eosinophils, also became perceptible and many of these cells disappeared from the splenic pulp and bone marrow. From ten days to three weeks later more or less regeneration of the lymphoid tissue became evident.

Since the time of these observations Heineke's re-

sults have been confirmed by many investigators, including Krause and Ziegler,²³ Fromme,⁸ Hall and Whipple,¹¹ Warthin,⁴⁸ Tsuzuki,⁴² and many others. Warthin's description of the effect of roentgen rays corroborated the observations of Heineke in every particular, except that by examining the tissue soon after irradiation Warthin found unmistakable evidence of the disintegration of lymphocytes within fifteen minutes after exposure of the animals to the rays, and a continuation of the cellular degeneration for several days. Similar effects have been obtained with radium. Other investigators have demonstrated that the lymphocytes in the circulating blood are equally sensitive to irradiation and that the circulating polymorphonuclear and eosinophilic leukocytes are on slightly less sensitive than the lymphocytes.

The rate at which the varieties of leukocytes mentioned are destroyed by irradiation under experimental conditions corresponds closely to the rate at which acute inflammations subside after exposure to a suitable dose of roentgen rays or radium. The only other cells in the body which are affected at anything like the same rate as the mucus-secreting epithelial cells in the salivary glands, the bronchi and the intestine, but since these cells cannot play any part in the majority of inflammatory processes, they may be excluded from consideration.

In circumscribed inflammations the significant role of lymphocytes, polymorphonuclear cells and eosinophils in the defense of the organism against infection and the sensitiveness of these cells to irradiation make it appear likely that when an inflammatory lesion is irradiated, the rays act mainly by destroying a proportion of the leukocytes infiltrating the lesion or circulating in the blood vessels which supply the affected region. This view is corroborated by the rapidity with which the symptoms often abate and the physical signs disappear. Moreover, microscopic examination of irradiated inflammatory lesions has repeatedly shown destruction of leukocytes, especially lymphocytes, to be the outstanding feature observed. It seems logical to conclude, therefore, that destruction of leukocytes is the primary and direct effect of irradiation. As a result of the disintegration of infiltrating leukocytes the antibodies, ferments and other protective substances which these cells contain are liberated in the surrounding tissue spaces, where they become mixed with the tissue fluids. It is also probable, as the experimental evidence indicates, that the next step is an increase in phagocytosis by reticular cells which become macrophages. No doubt other intimate, secondary or indirect effects related to cell metabolism are pro-

duced but the precise character and significance of these effects are not clear.

Since leukocytic infiltration is an outstanding factor in the defense against infection, the natural question is why destruction of a large number of leukocytes infiltrating such lesions may not do more harm than good. The only answer is that, after small or moderate doses no one has yet submitted any evidence of ill effects. The influence of irradiation has always been favorable or the rays have failed to alter the course of the inflammatory process.

From the foregoing considerations, therefore it seems not unreasonable to assume that irradiation, by destroying some of the infiltrating leukocytes, causes the protective substances in these cells to be liberated and to be made even more readily available for defensive purposes than when they were in the intact cells. This and the increase in phagocytosis which follows the disintegration of the cells represent the main effects of exposure to roentgen rays or radium, and probably explain the usually favorable action of these agents.

All the clinical circumstances indicate that in inflammatory lesions respond to irradiation in proportion to the degree of leukocytic infiltration. In favor of this view are the experimentally proved radio-sensitivity of lymphocytes, polymorphonuclear leukocytes and eosinophils, the fact that the rate of regression of acute inflammations corresponds to the rate at which these cells are known to be destroyed by irradiation and the fact that these cells are the only ones commonly found in inflammatory lesions that could be affected at such a rapid rate by small or moderate doses. Other circumstances pointing in the same direction are that radiotherapy is more beneficial during the infiltrative stage and less so during the suppurative stage, and that, although the majority of lesions yield quickly to treatment, some respond less rapidly or do not respond at all. Variation in the degree of leukocytic infiltration of different lesions of the same character or of similar lesions of different character is a well known pathological fact. Therefore, the degree of leukocytic infiltration must influence the action of the rays, because the rays can destroy leukocytes only in proportion to the number of these cells. This is undoubtedly related to and probably explains the fact that, while many inflammatory lesions are influenced favorably, some react much less or not at all.

When the inflammation is not confined to a small region but is extensive or diffuse rather than circumscribed and when leukocytic infiltration is not a pronounced feature, as in erysipelas the rays probably act in a somewhat different

manner. Under these circumstances, the smaller number of infiltrating leukocytes should prevent the rays from having the same local effect, unless some compensatory mechanism enters into play. Evidence of such a mechanism in erysipelas has not yet been demonstrated, but that it exists is indicated by the action of roentgen rays in other diseases. In bronchial asthma, for example, irradiation of the spleen or of other parts of the body remote from the bronchi and lungs is often followed by more or less striking relief from symptoms. What probably takes place is a destruction of leukocytes in the spleen and in the large mass of blood circulating through this organ. Then the cellular debris and the contents of the destroyed cells find their way into the general circulation, where they have been shown to produce a protein-like reaction. In inflammations that are not circumscribed and in which leukocytic infiltration is comparatively slight the affected region is hyperemic and the vessels are more or less gorged with blood. Wide exposure of such a region to a small dose of rays undoubtedly causes many leukocytes to disintegrate, and the contents of the destroyed cells are liberated into the blood and throughout the tissue spaces. And the destruction of leukocytes is probably followed by changes similar to those described in connection with more limited inflammations. At least this would seem to be the most logical conclusion. Any other assumption would be inconsistent with the known facts and with the clinical behavior of this kind of inflammation.

Recently, a well known radiologist told me that he thought the action of the rays must be on the hyperemia and the edema. According to this conception the rays would act on the serum in the blood or tissues and not on the cells. If this were true, the action of the rays would necessarily be chemical or physicochemical. But where is the evidence to support such an idea? I am not aware of any. On the contrary the evidence in favor of a direct and major action on infiltrating leukocytes is so abundant that anyone who takes the trouble to analyze and correlate it cannot fail to be impressed with its probable significance.

Chronic Inflammations. In order to understand the influence of irradiation on chronic inflammations it is necessary to bear in mind a few essential points. Depending on their character and on the etiologic factors which produce them such lesions are characterized by varying degrees of leukocytic infiltration, connective tissue proliferation and caseous, calcareous or hyaline degeneration. Moreover the clinical effect of irradiation is slow and maximal improvement or cure requires repeated treatment at intervals. From what

is known about the action of roentgen rays and radium on different varieties of cells and tissues, it seems most likely that these factors are closely related. Since cheese and chalk are products of cellular degeneration, they should not be influenced by irradiation, and this is precisely what is observed in practice. As we have already seen, the varieties of leukocytes which are such an important feature of inflammatory infiltration are exceptionally sensitive to roentgen rays or radium. Connective tissue cells, on the contrary, are comparatively resistant to irradiation; they are even less sensitive than the epithelium of the skin. In this respect the difference between lymphocytes or polymorphonuclear leukocytes and connective tissue cells is tremendous.

Analysis and correlation of these several factors would seem to furnish a satisfactory explanation of the effect of radiotherapy on chronic inflammatory processes. The greater the degree of leukocytic infiltration in proportion to connective-tissue proliferation, the more marked and the more rapid is the influence of the treatment, and vice versa. If tuberculous lesions are taken as an example, it is well known that the effect of irradiation is greater during the infiltrative phase of the tubercles, when leukocytic infiltration is most pronounced, than it is when the leukocytic infiltration has diminished and has passed into an advanced stage of caseous degeneration or of repair by connective tissue or by calcification. It is probable, therefore, that leukocytic infiltration, on the one hand, and connective-tissue proliferation, on the other, act in opposite directions, the former tending to increase the effect of irradiation and the latter to diminish or retard this effect. This conclusion is in complete harmony with the experimental evidence and with all the clinical observations which have been recorded.

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DISCUSSION

DR BENJAMIN PARVEY, Boston. I should like to ask Dr Desjardins if he can tell us anything about the treatment of pilonidal sinus by x ray.

DR HERMAN A. OSGOOD, Boston. I should like to ask Dr Desjardins whether sulfanilamide should be administered simultaneously with x ray in acute infections. There are so many new conditions that Dr Desjardins has brought up from the standpoint of x ray treatment—that is, conditions new to us—that there should be a considerable field for discussion. Perhaps Dr Desjardins will add a little more detail as to the treatment of pneumonia, about which we have heard a good deal.

A MEMBER Can Dr. Desjardins tell us anything about the treatment of phlebitis?

DR. DESJARDINS I am glad the question about phlebitis was brought up. We have treated quite a number of cases of acute phlebitis. Some of them do very well in fact a majority do well; but here again it is very important to treat widely. If, for instance, the phlebitis affects a lower extremity the entire extremity and portions of the lower part of the trunk should be treated. Trying to treat only a patch on the leg where the condition is worst is not likely to yield the best result. When phlebitis is treated early, as soon as the diagnosis is made, it is surprising how well this kind of inflammation responds. On the other hand if treatment is started late, the results are not so gratifying.

As for the possible advantage of combining sulfanilamide with roentgen ray treatment, this new group of drugs has put an entirely different face on the treatment of certain infections, and this must be taken into account. What I have said about roentgen ray treatment was based on work done before the days of sulfanilamide. There

is no question that some of these drugs have effects which are so striking that there is no dodging our responsibility to make use of them and in certain cases I should not take the position that roentgen rays should be utilized to the exclusion of sulfanilamide or similar drugs. We should employ every remedy available, and if the condition yields as well to sulfanilamide, by all means it should be used and continued until the case is cured. On the other hand if a case does not respond well to sulfanilamide or the response is not so good as one would expect, I should not hesitate to use roentgen rays also. In pneumonia if roentgen rays are to be employed at all they should be used as soon as the diagnosis is made. To postpone their use until later is to rob them of part or all of their possible efficacy.

I have had no experience with the treatment of pilonidal sinus with roentgen rays although I am aware that reports of good results have been published in the literature. I have not had a single case in which to test this method and without having had an opportunity to try it in fifty or a hundred cases I should not venture to express an opinion.

SULFANILAMIDE IN THE TREATMENT OF ERYSIPELAS*

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FOLLOWING the introduction of sulfanilamide as a chemotherapeutic agent in the treatment of hemolytic streptococcus infections, reports have appeared describing its use in the therapy of erysipelas. It has seemed worth while to review this material and to present the data from cases treated at the Boston City Hospital in which the drug has been administered.

The disease, characterized by a red, spreading, indurated lesion of the skin, most frequently involving the face and often complicating operative wounds, has been shown to be caused by streptococci which are immunologically and culturally members of Lancefield's Group A, but of no particular serological type.¹ The organisms can usually be recovered from the local lesions, where they have been found histologically to be confined to the lymphatics and to spread through them.

The facial type is frequently preceded by either acute or chronic upper respiratory infection, and in these cases the organisms can regularly be recovered from the nose, from which they have been transferred to the surrounding skin, invading it through minute excoriations. The onset is most often acute and frequently accompanied by chills, and is followed in one to three days by the appearance of the skin lesion, the diagnosis being delayed

until the third day in as many as 30 per cent of cases, owing to the late appearance of the lesion.² Only a very few cases are afebrile, high fever persisting for four to ten days being the rule. Fall of temperature is by lysis or crisis, frequently the latter, and occurs oftenest on the sixth to eighth day, in an average of 7.9 days.² The clearing of the skin lesion lags behind this event for several days. The mortality rate varies with the age of the patient and with the presence of chronic debilitating disease. Below the age of two, 50 to 75 per cent of all patients may be expected to die, and beyond the fifth decade there is a sharp rise in the percentage of fatal cases. Between these two groups the death rate is less than 5 per cent. Seegal and Seegal³ have pointed out that in 85 per cent of their fatal cases there was some underlying disease of a serious nature and Keefer and Spink,⁴ at the Boston City Hospital, found that in 80 of 220 fatal cases there was some such condition. The presence of a blood culture positive for the hemolytic streptococcus is of grave prognostic significance. Nearly all the infants in whom this sign has been positive have died.

Complications in the course of the disease other than local abscess, cellulitis or necrosis of the skin are uncommon but bronchopneumonia, nephritis and meningitis occur.

Recurrence of attacks similar to the first occur after varying time intervals in many individuals, and some patients seem to become permanently

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more susceptible. Some cases have a relapse ten to twenty days after the onset of the disease, when recovery seems to be firmly established. Patients displaying this phenomenon have been shown to be divisible into two groups, those who have organisms demonstrable at the local lesion, in many cases with a high titer of circulating antibody, and those who have no demonstrable organisms but react to bacterial products, presumably on the basis of local hypersensitivity of an allergic nature.⁴

Of the many articles in the literature discussing the use of sulfanilamide in the therapy of erysipelas, the following are the most significant.

Peters and Havard⁵ have treated 47 cases with sulfanilamide, in all of which the spread of the lesions was arrested within twenty-four hours and the temperature returned to normal within forty-eight hours. No other details or control series are mentioned.

Snodgrass and Anderson⁶ present a detailed study of 106 cases treated with Prontosil and a control group in which ultra-violet light was used alone. No spread of the lesions was observed after twenty-four hours in 82 per cent of the drug-treated cases, whereas this result was achieved in only 59 per cent of the controls in the same time. In 76 per cent of the former the temperature was normal within forty-eight hours, this occurred in only 48 per cent of the latter. Recurrences, complications and deaths were of the same order of magnitude in both groups.

Hageman and Blake⁷ administered sulfanilamide to 27 patients and compared the results with a similar number studied the year before in the same hospital. The febrile duration of the disease was 13.9 days in the control and 5.3 in the treated series, recovery in the latter occurring on an average 2.2 days from the onset of therapy. Two infants under ten days of age with positive blood cultures recovered. The usual dose was 4 or 5 gm per day. Infectious complications occurred in 3 cases and recurrence in 1. Of 3 deaths, none seemed directly attributable either to the infection or to the sulfanilamide.

Meyer-Heine and Hugenin⁸ regard the drug as a specific therapeutic agent in this disease, its exhibition by mouth being followed in 148 of 150 cases by a rapid fall in temperature and subsidence of the local lesion within forty-eight hours. There were no deaths, but local complications occurred in a number of cases. Bloch-Michel et al.⁹ have had a similar experience in 180 cases, except that there were 7 deaths, all of aged and debilitated patients. A dose of approximately 2 gm per day was used in both these investigations.

The temperature and pulse in 23 cases treated

by Kramer¹⁰ became normal in an average of 43 days against an average of 11.3 days for a comparable control group. The dosage was believed to be inadequate in the 2 cases which failed to respond to treatment. Eighteen of 22 cases followed by Frankl¹¹ showed a critical fall in temperature in the first or second twenty-four hours and the patients were fever-free within three days. Spread of the local lesion after forty-eight hours was observed in only 2 cases. Complications were present in all cases with prolonged fever, 1 death was noted, that of an old and debilitated man.

Breen and Taylor¹² administered 2 gm of sulfanilamide daily in a series of 35 cases of erysipelas and found that 33 regressed, with a return of the temperature to normal within forty-eight hours. There were 2 deaths, one of a patient who entered the hospital in a moribund state, and the other as the result of a cardiovascular accident.

Nelson, Rinzler and Kelsey¹³ treated 344 patients suffering from erysipelas with sulfanilamide and compared the results with those obtained by various other methods in over 4000 cases. The hospital stay was found to have been shortened from 110 to 70 days, the duration of fever from 6.8 to 4.2 days and the mortality rate from 80 to 15 per cent. In children the mortality rate was reduced from 19.7 to 12.9 per cent.

ANALYSIS OF CASES

We have studied without special selection all those patients admitted to the male wards with a diagnosis of facial erysipelas from October, 1937, to June, 1939—42 in all. As a control, the records of 43 similar patients admitted during 1936 and 1937 before the use of sulfanilamide was instituted have been evaluated. All received a standard therapy consisting of bed rest, fluids, sedatives and cold magnesium sulfate compresses on the affected areas. Those to whom sulfanilamide was administered received as a routine 6 or 8 gm by mouth in the first twenty-four hours, with a maintenance dose of 3 to 5 gm per day thereafter.

In so far as various factors existed which might influence the course of the disease, the two groups were roughly comparable. Advanced age has been shown to predispose to the severity of the infection,³ 50 per cent of the treated and 48 per cent of the control cases were in the fifth, sixth or seventh decade. Since debilitating disease also tends to modify the course of the disease unfavorably, the cases were examined in order to determine its presence. Fourteen, or 33 per cent, of the controls were found to be suffering from serious chronic disease. These were predominantly chronic alcoholism, marked generalized and cere-

bral arteriosclerosis, congestive heart failure and rheumatic heart disease, there was 1 case of diabetes mellitus. In the treated group 13 patients, or 30 per cent, were found to have similar conditions, chronic alcoholism or cirrhosis of the liver occurred in 8, and fibroid pulmonary tuberculosis, lentic heart disease, chronic osteomyelitis of the hip, postencephalitic Parkinson's disease and rheumatoid arthritis each in 1 case. The blood cultures of all patients were negative when this examination was made, except for 1 case in the controls which was positive for a hemolytic streptococcus and 2 cases in the treated group one positive for *Staphylococcus aureus* and the other for a hemolytic streptococcus, all patients with positive cultures died.

As criteria for the evaluation of the effect of the drug we have considered the duration of fever, the incidence of complications and the mortality. It has proved impossible to use the subsidence of the skin lesions as such a measure because of insufficient data in the untreated cases.

The duration of fever from the onset of illness in the control group averaged 7.5 days, as compared with 7.1 in the treated cases, the former having extremes of four and twenty-three days, the latter of two and nineteen days. After the beginning of sulfanilamide therapy 8 patients were afebrile within twenty-four hours, 13 within forty-eight, 6 within seventy-two and 12 after seventy-two. If the time of institution of therapy is considered in relation to the onset of the disease, it is found that of 21 patients treated on or before the third day of illness the total febrile course averaged 5.2 days, with an average of 3.0 days after beginning the drug. In cases in which the drug was given after the third day fever persisted for an average of 9.1 days and subsided in an average of 4.2 days after the onset of medication.

The total duration of fever was therefore markedly shortened in those patients treated on or before the third day of the illness. In those treated after this interval the average febrile period was longer than in the control group. The course of the illness in these individuals was more severe, and an average of twenty-four hours more elapsed before the temperature reached normal after exhibition of the drug. Fever continued for more than ten days in 7 of the latter patients, and in only 2 of those treated early.

Complications were present in 7 of the untreated patients and 9 of the treated. Of the former 3 or 7 per cent, had a recurrence, a similar number had abscess of the face. 1 had bronchopneumonia and 1 acute purulent otitis media. Of the latter group 2, or 5 per cent, suffered recurrence. 4 or

10 per cent, developed abscess of the face. 1 had a toxic hepatitis, and 1, bronchopneumonia.

It is therefore impossible to demonstrate any important difference in the complication rate between the two groups. Of those patients who received sulfanilamide early in the course of the disease, suppurative complication occurred in only 1 (abscess of the eyelid), but 2 suffered relapse.

There was 1 death in the untreated series, a mortality rate of 2 per cent distinctly lower than the 16 per cent previously reported from this hospital.¹¹ Three deaths occurred among the treated cases, a rate of 7 per cent. These cases require special comment.

CASE 1. A 73-year-old man admitted to the hospital with a 2-day history of swelling of the face, was found to suffer from typical facial erysipelas complicated by arteriosclerotic heart disease, with auricular fibrillation and chronic pulmonary fibrosis of unknown etiology. The temperature was 100 F. and the pulse 80. Sulfanilamide was immediately exhibited by mouth and 6 gm. was given in the first 12 hours. In spite of this treatment the giving of digitals, and the usual supportive therapy the patient became irrational, the temperature rose to 105 F., and death occurred 24 hours after entry. A blood culture was positive for a hemolytic streptococcus.

CASE 2. A 32-year-old man was admitted to the hospital with a history of coryza and sore throat of 3 days duration and swelling of the face for 24 hours. He had had two previous admissions to the hospital because of marked cardiac failure due to rheumatic heart disease with mitral stenosis. He was found to have the lesions of facial erysipelas and the signs of cardiac enlargement and mitral stenosis without decompensation. The temperature was 100 F., and the pulse 90. The blood culture was sterile. Six grams of sulfanilamide was administered in the first 24 hours, but pulmonary edema ensued and the patient died 24 hours later in acute peripheral vascular collapse.

CASE 3. A 42-year-old man was admitted to the hospital with a history of swelling of the face for 6 days following a cold. He had used large amounts of alcohol over a long period of time. He was found to be suffering from extensive erysipelas involving the face, scalp and neck. A blood culture was positive for *Staphylococcus aureus*. The temperature was 104 F., and the pulse 100. The oral administration of sulfanilamide was begun in doses of 2 gm. every 6 hours but after 4 gm. had been given the patient developed profound peripheral vascular collapse and died.

These cases are presented in order to illustrate that certain individuals suffering from changes of old age, arteriosclerosis, heart disease, chronic alcoholism or some other debilitating disease will continue to die as the result of an acute infectious process such as erysipelas, even though sulfanilamide be exhibited as soon as the patient comes under the care of the physician. It is important

to point out that one of these patients was treated on the second and one on the third day of his illness. It cannot, therefore, be said that early treatment leads in every case to a satisfactory termination of this disease. The third patient, treated first on the seventh day, with a complicating *Staphylococcus aureus* septicemia, could not have been expected to recover.

Few untoward side effects were observed as the result of the use of sulfanilamide except cyanosis and headaches. Anemia and agranulocytosis did not occur, but dermatitis was observed in 1 case, and several of the more prolonged fevers may have been due to the presence of this drug in the body of the patient.

DISCUSSION

The mode of action of sulfanilamide and its relation to recovery in erysipelas require comment. Although the exact immunologic processes involved in recovery in this disease have never been fully elucidated, the work of various investigators has in part clarified the picture. Birkhaug¹³ has reported a circulating soluble toxin obtained from the hemolytic streptococcus, and believes that development of antitoxin in the blood must precede the recovery process, a thesis which Francis¹⁶ was unable to confirm. The latter postulates the development of allergy to bacterial products, followed by the appearance of an antiallergin as a prerequisite to the recovery state. Local tissue immunity of the skin has been suggested and in part demonstrated experimentally by Gay and Rhodes¹⁷ and Rivers and Tillett,¹⁸ but has not been demonstrated in the infected human subject. Spink and Keefer⁴ were able to demonstrate the presence of immune bodies against the hemolytic streptococcus in the form of antistreptolysin, antifibrinolysin and increased bactericidal power of whole blood for this organism. In some cases these were present in marked degree when the patients were first seen, but in others they were observed to increase in amount during the disease and to fall away after recovery had taken place. In certain cases with recurrence, organisms could not be demonstrated in the local lesions but typical attacks could be induced by the subcutaneous injection of toxic filtrates of the organism, suggesting that the reaction was one of response of sensitized tissues to bacterial products.

In the light of the above studies, it seems fair to conclude that antibacterial and perhaps antitoxic antibodies both humoral and of the local tissues, and local sensitivity of an allergic nature all play a role in the recovery from the disease, and that the latter event does not occur until some of these products have reached a high level

which is maintained long enough to sterilize the local lesion.

The mode of action of sulfanilamide has been repeatedly shown to be that of bacteriostasis, with almost no bactericidal effect in various media in vitro. We⁸ have shown that this is also true of whole blood, and the data suggest that the drug possesses increased effect in bloods with a high antistreptococcus antibody titer. It has also been shown by Colebrook et al.,¹⁰ Long and Bliss²⁰ and us¹⁴ that in mouse protection tests the animals survive only so long as the drug is present in adequate concentration, and that after its withdrawal most of the animals succumb, presumably because they have failed to develop any natural immunity against the organism, which has been inhibited but not killed by the drug.

From these observations it would seem that sulfanilamide cannot be expected to effect immediate cures of erysipelas. It should be expected that it will slow the rate of multiplication of the organism, and thus prevent some of the destructive local effects and decrease the rate of spread through the lymphatics, but a fall in temperature and subsidence of the local lesion must presumably await the development of antistreptococcus immune bodies in the afflicted individual. That this is so is indicated by the previously recorded data, since a fall in temperature has rarely occurred in less than forty-eight hours after the administration of the drug by mouth, and the average course in the group treated early has been about five days. Neither should sulfanilamide be expected to prevent that type of relapse with sterile local lesion and hypersensitivity to bacterial products, since no action affecting this kind of reaction has been demonstrated.

It is difficult to draw any definite conclusions from the above observations as to the efficacy of sulfanilamide in the treatment of erysipelas. The previously published data are on the whole, insufficient and without controls, but all authors have believed that the drug was a useful adjunct in the treatment of this condition.

The data presented in this paper suggest that the duration of the disease is shortened markedly when the drug is given on or before the third day of the illness. Clinically these patients have a mild disease and a short convalescence. After the third day it has been impossible to demonstrate any effect of this agent on the course of erysipelas. This is to be expected, because by the fourth day the local lesions are usually fully developed and relief by the natural mechanisms of the body must be awaited. In cases treated early the circumstances are different, as the infection is still spreading through the skin, and

it may be possible to curtail markedly the area involved in the local lesions as well as the toxemia by the use of sulfanilamide, thus mitigating the severity of the disease and limiting its extent and duration.

No difference in the complication rate has been demonstrated by this or any previously reported study, and the incidence of death is so low as to be an unreliable approach in the case of adults. The fact that infants under six months of age with blood cultures positive for the hemolytic streptococcus have recovered is encouraging, and suggests the efficacy of the drug against this organism.

On the whole, the therapeutic results of the use of sulfanilamide in facial erysipelas seem sufficiently encouraging to continue its routine use in the treatment of this disease, with emphasis placed on its administration in adequate dosage as early as possible after the onset of the illness.

SUMMARY AND CONCLUSIONS

The effect of sulfanilamide on the course of facial erysipelas has been studied in 42 cases and compared with 43 similar cases treated previously.

The drug is found to shorten the course of the illness and to decrease its extent and severity if it is administered before the third day of the disease. It has little effect after this interval.

Complications occur frequently in the treated cases, but less often in those treated early.

Recurrences and relapses occur among the treated cases as often as among the untreated group.

Death occurs in certain aged or chronically ill patients even though sulfanilamide is administered early and in adequate doses.

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SUPPRESSION OF URINE COMPLICATING PYELOGRAPHY*

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THE development of the newer synthetic organic compounds containing iodine has furnished the urological and roentgenological armamentarium with pyelographic materials of great value. By their use, injected either intravenously or through a catheter passed into the ureter, excellent, highly informative shadow outlines of the urinary tract are obtained in the x-ray film. The use of the intravenous method of injection has become especially widespread, for by this means it is often possible to avoid the discomfort attending the use of the cystoscope.

The materials generally used today for excretory pyelography are Skiodan (sodium mono-iodo-methane sulfonate), Diodrast, also called Neo-skiodan or Iopracyl (3, 5 diiodo-4-pyridone-N-acetic acid dissolved with diethanolamine), and Hippuran (sodium ortho iodo hippurate). Each of these organic iodine compounds is opaque to x-rays, and after intravenous injection appears quickly and in high concentration in the urine. Experimentally, and in clinical use as well, each is found to be treated by the body as an inert foreign material which is for the most part quickly excreted unchanged by way of the urine. The iodine though large in amount, is firmly bound on theoretical grounds the union of the iodine atom with hippuric acid, which itself is a normal product of metabolism, would seem to furnish a substance more apt to be well tolerated by the body than when the iodine is united with more complex forms. In clinical use, however, no demonstrable superiority of any one of these substances over the other has been experienced.

Recently, Diodrast and Hippuran have been studied by physiologists with regard to their passage through the kidney.¹⁻⁴ It is found that these substances are promptly taken out of the blood stream by the renal tubules to appear in high concentration in the tubular urine. The suggestion follows that by their use it may be possible to measure renal blood flow, and at the same time to differentiate tubular function and that of the glomerulus.

In view of the very appreciable amount of work thrown on the cells of the renal tubules by the injection of these foreign pyelographic substances into the blood stream, it might be expected that untoward effects would be noted occasionally,

especially in cases where the kidney tissue was the site of previous disease. But such account appear very rarely indeed in the literature.

In 1936 Cumming and Chittenden⁵ studied the subject of intravenous and retrograde urography by means of a questionnaire. They report the following unfavorable or "allergic" reactions to the intravenous injection: urticaria, rhinitis, lacrimation, salivation and edema of the glottis. Many of these manifestations are those seen in the state of iodism after the administration of some such drug as potassium iodide. Here the effects may be of toxic origin caused by the drug itself, but since many patients can take iodides for long periods without showing unfavorable reactions, whereas some respond by a severe coryza after only twenty-four hours, it is likely that here too allergy may play a part. In Cumming and Chittenden's report, a few cases of slight transient anuria following intravenous injection are noted, with out further comment.

As concerns the retrograde injection of pyelographic media into the renal pelvis, the earlier literature contains an occasional report of a death seemingly so caused. We are unable to find any such reports when Skiodan, Diodrast or Hippuran was used. It is to be noted in this regard that there is always some absorption from the renal pelvis into the blood stream of whatever substance is injected into it through the ureteral catheter. It has been shown also that this retrograde absorption, the so-called pyelovenous or pyelolymphatic reflux, takes place without there being caused any significant increase of the intrapelvic pressure at the time of injection. An interesting illustration of this fact has lately been seen by us after pelvic injection of a solution of the maltoside of sulfanilamide in order to combat renal infection in patients who were unable, for one reason or another, to take the drug by mouth. In such cases we were able to demonstrate sulfanilamide in the blood stream in appreciable amounts shortly after injection.⁶ Further, at operation on a kidney free from infection, of which a pyelogram has been made by retrograde injection the day previously, one frequently notes an edema of moderate amount involving the fatty tissue immediately surrounding the renal pelvis. In the absence of other probable explanation such circulatory interference has always been thought by us to be a result of the recent intrapelvic injection.

From all evidence at hand, therefore, it is probably fair to assume that a portion of whatever

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is injected into a renal pelvis will reach the blood stream.

It is doubtless true that any substance however innocuous, used for pyelography places a burden on the kidney. When the substance is used in the form of intravenous and retrograde injections at the same time, or in the presence of a diminished renal excretory power as when the function of one kidney is temporarily suspended serious embarrassment of renal function may follow. The following cases are in point.

CASE 1 (No 48863) A 53-year-old man suffered an attack of sharp pain in the region of the left groin which persisted intermittently for 2 days. Three years before this he had had treatment for a duodenal ulcer which was continued in the form of alkalies and diet during the following 2 years. The suggestion that the present attacks of pain were due to a urinary calculus formed under this regime was considered likely.

Examination showed that the urine contained a few red and white blood cells and a large amount of crystalline material in the form of triple phosphates. X-ray films failed to reveal any shadow suggestive of calculus but urine delivered through a ureteral catheter on the right side showed a few white blood cells while that from a catheter on the left contained blood. The course of the ureteral catheters as seen in the x-ray film together with the presence of a soft-tissue shadow suggested to the urologist the possibility of a horseshoe kidney. Following this examination the daily output of urine was normal amount. Two days later it being found impossible to pass a catheter up either ureter because of edema of its orifice an intravenous injection of 20 cc. of Diadrast was made. No excretion of this material into either renal pelvis occurred, and during the following 2½ days no urine was formed. The patient perspired freely complained of discomfort in the lower portion of the abdomen and became increasingly drowsy. Forty-eight hours later he began to vomit. The nonprotein nitrogen of the blood measured 73 mg. per 100 cc. at this time and later reached 112 mg. Under active treatment by enemata, hot packs and intravenous saline solution containing glucose, renal secretion began again after a cessation of nearly 3 days. Subsequent tests of renal function showed a prompt return to normal so that at the end of 2 weeks the patient was able to return home apparently well in every respect. The condition of the kidneys was investigated 4 months after the above episode and again 2 years later. Normal clearance and normal amounts of nonprotein nitrogen in the blood were found.

CASE 2 (No 57693) A 57-year-old man was seen 3 hours after the onset of an attack of colic and pain in the left flank accompanied by dysuria and urgent urination. The left kidney appeared to be slightly enlarged. The lower pole being easily palpable but non-tender. The urinary sediment showed many red blood cells. The non-protein nitrogen of the blood was 26 mg. per 100 cc. A presumptive diagnosis of left-sided renal colic due to calculus was made and the patient was put to bed and given salicylates. Urological investigation the following day showed the left ureter patent as far as the renal pelvis. The fluid from the left kidney contained red blood cells, but no pus or bacteria. X-ray films showed a small poorly visible shadow at the tip of the ureteral catheter in the renal pelvis. Six cubic centimeters of a solution of Hippuran was used in order to make a retrograde pyelogram. Examination of this showed a somewhat irregular out-

line of the renal pelvis. No uncomfortable reaction followed the pyelography and the next day excretory urograms were made so as to get a comparative film of the pelvic abnormality. The outline of the right renal pelvis 5 minutes after injection was well visualized and was normal. There was delayed excretion and poor concentration of the opaque medium from the left kidney making visualization of the calices and pelvis unsatisfactory. Immediately after intravenous urography the patient passed about 25 cc. of blood-tinged urine, but after this passed no urine for 74 hours. He gradually grew more drowsy and had a sensation of tension or fullness in each flank. During 48 hours he was able to take some fluid by mouth but during the 3rd day he vomited. There was no pulmonary or peripheral edema but the temperature was as high as 101 F. He received over 5000 cc. of fluid each day mostly in the form of saline solution containing 5 per cent glucose. During the 3rd day he was also given 100 cc. of a hypertonic (10 per cent) solution of sodium chloride intravenously. The nonprotein nitrogen of the blood reached a level of 96 mg. per 100 cc. At the end of the 3rd day 30 cc. of bloody urine was passed, followed an hour later by 75 cc. and during the next 18 hours there was passed over 6000 cc. of urine, which contained less blood on each urination. A day later the urinary sediment showed both white and red blood cells in moderate number and an occasional granular cast. Two days after the kidneys had begun to act again they were found to excrete 70 per cent of a solution of phenolsulfonephthalein in the 1st hour and 20 per cent in the 2nd. A concentration test showed a maximum specific gravity of 1.020 and a minimum of 1.010. Nine days later a divided functional test of the kidneys through the ureteral catheters showed excretion values of 13 per cent phenolsulfonephthalein from the right kidney and 17 per cent from the left in a 10-minute period. The urine still contained a slight trace of albumin. After returning home this patient was investigated by his physician for evidences of nephritis but none were present. A year after the above episode he was again seen by us. He reported excellent health in the meantime and the urine was normal.

CASE 3 (No. 60326) A 35-year-old man came to the Emergency Ward complaining of steady pain in the right flank during the previous day. There had been no colic. Examination showed a temperature of 100 F and a white cell count of 14,000. The region of the appendix was not remarkable, but slight tenderness was present in the right costovertebral angle. The urine contained red blood cells in small numbers and an occasional white cell. A plain x-ray film of the urinary tract failed to show any shadow suggestive of stone. Six hours later the temperature having risen to 101 F., the patient was admitted to the hospital for observation. Twelve hours later the temperature had returned to normal but the white-cell count was still elevated. There was continued pain in the right side. Intravenous pyelography with 20 cc. of Diadrast gave urograms in which the left kidney pelvis was outlined promptly and appeared normal. For as long as 30 minutes after injection no shadow appeared on the right side, there being no excretion. Although nothing suggesting the shadow of a calculus could be seen it was thought that the patient's ailment probably lay in a right ureteral calculus blocking the kidney and transparent to x-ray. A cystoscope was therefore passed and the right ureter was catheterized. The efflux was noted to contain blood before the catheter was inserted. About 3 cm. above the bladder a partial obstruction was encountered after the passing of which a profuse flow of urine was obtained through the catheter. Beyond this point no further im-

pediment was found as far as the renal pelvis. Exploration of the left ureter revealed no abnormality. A divided function test with phenosulfonephthalein showed each kidney to be normal in its excretory power. A retrograde injection of 5 cc. of Hippuran was made into the right renal pelvis, and stereoscopic x-ray films were taken. These showed the right renal pelvis of normal size and contour. The faint shadow of a calculus was present in the lower third of the ureter, the stone apparently lay adjacent to the catheter and at or somewhat above the point at which the passage of the catheter had encountered resistance.

On the theory that relief of obstruction of the right kidney was indicated, the ureteral catheter was allowed to remain in place. It was removed, however, after 2 hours because, although its lumen was patent, no urine flowed through it. At this time the patient passed about 50 cc. of somewhat bloody urine from the bladder, but did not void again for 76 hours. His course during this time was stormy. Besides the presence of distention, nausea and vomiting, the white blood cells were markedly increased in number, there were several chills followed by high fever and a culture of the blood showed the presence of *Staphylococcus albus*. Nevertheless the kidneys eventually responded to forced intravenous fluids together with enemas, so that on the day following the period of anuria 2500 cc of urine was passed.

During the next 5 days large amounts of urine were passed, but the temperature remained elevated. The patient's appearance had improved, but there was still considerable tenderness over the right kidney. The right ureter was therefore re-examined by catheter. The area of obstruction was again encountered, and the urine from the right kidney showed considerable pus and *Staphylococcus albus*. The left kidney seemed to have normal function and to secrete a sterile urine. On the 14th hospital day the patient was subjected to operation, at which a thickened, scarred area in the ureter was found 3 cm. above the great vessels. This area was 2 cm. long, and around it the periureteral tissues showed distinct adhesions and induration. Incision demonstrated an inflammatory stricture, no stone was present. The stricture was dilated to No. 12 French, and drainage was instituted. Convalescence was uneventful, but the obtaining of a positive culture for *Bacillus coli* from the urine made necessary a subsequent course of sulfanilamide. The patient recovered but has continued under observation in the ambulatory clinic. No doubt further dilatation of the ureteral stricture will be necessary.

CASE 4 A somewhat obese man of 48 underwent cystoscopic examination in a neighboring city to determine the cause of an intermittent though marked hematuria, first noted 3 weeks earlier. Previously he had been entirely well. A papillary growth of considerable size was found overlying and obscuring the right ureteral orifice. A retrograde pyelogram of the left renal pelvis was made, using Skiodin. Since a similar evaluation of the right renal pelvis was impossible, the usual amount of a solution of Diodrast was injected into a vein of the arm. X-ray films obtained by these means showed a normal renal pelvis of the left kidney in both the retrograde and excretory urograms. The right pelvis failed to fill, and so was not visible in any of the films made after intravenous injection. It was therefore concluded that the hematuria was due to a papillary carcinoma of the bladder involving the right ureteral orifice and causing loss of renal function in the kidney above. The left urinary tract and kidney were normal.

Following these examinations increasing distention of the abdomen, vomiting and gradual suppression of urine occurred. The patient was seen in consultation 3 days

later. At this time the bladder was still empty, in spite of the previous administration of mercurial diuretics and one small intravenous injection of saline solution containing 5 per cent glucose. The sensorium was not clouded, there was only moderate fever and the pulse was of good quality, although somewhat elevated. A Wangensteen tube which had been adjusted so as to control vomiting could not be tolerated. No evidence of edema was seen, and palpation of either kidney was made impossible by soft distention of the abdomen.

Advice was given to omit all mercurial diuretics and to force fluid in the form of intravenous injections of saline solution in 500-cc amounts up to 5000 cc. daily, the first injection to contain 10 per cent glucose and the others 5 per cent. Under this regime the urinary suppression ceased after a day, at the end of 36 hours urine was being secreted copiously and the patient's general condition was again normal.

DISCUSSION AND CONCLUSIONS

It is to be noted that in each of these cases injections of urographic mediums were made by both the intravenous and retrograde methods. The injections followed each other immediately in 2 cases, and within twenty-four hours and forty eight hours respectively in the others. Complete cessation of urine occurred immediately after the second injection. After anuria for various periods, seventy-six hours in the most marked case, the kidneys resumed their function, having been stimulated in the meantime by copious injections of saline solution containing glucose. In only 1 case was there evidence of infection. Before investigation each of the patients presented either partial or complete inhibition of the function of one kidney, in 3 cases this was caused by the passage of a small calculus, and in 1 by a neoplasm of the bladder. The unobstructed kidney was apparently normal at this time. In 3 cases subsequent study of the kidneys at various times following the occurrence of the period of anuria demonstrated no evidence of nephritis.

It is evident that suppression of urine of severe and alarming degree may follow the injection of the usually innocuous pyelographic mediums when these are used in an amount too large to be passed successfully through a normal single kidney. No signs of toxicity occurred in the series other than those due to the cessation of renal function.

In the light of these experiences it seems wise in cases of unilateral or bilateral reduction of normal renal function to repeat pyelographic studies, especially by both the excretory and retrograde methods, only after a forty-eight-hour interval.

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NEUROSYPHILIS AND ITS TREATMENT*

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IT IS a regrettable fact that discussion of syphilis of the nervous system and its treatment is still necessary. This, of course, would not be so if every patient with primary or secondary syphilis were promptly and adequately treated. It is the aim of the medical profession and the public health service to eradicate syphilis. The means to accomplish this aim are at hand, but as yet there has been insufficient education of the public in regard to the necessity of proper treatment and public-health measures, and the medical profession is not sufficiently conversant with what constitutes adequate treatment. Syphilis at the present time is the direct cause of 5 or 10 per cent of all new admissions to psychopathic hospitals,¹ and of an equal percentage of admissions to general neurological wards. Even if our most optimistic hopes are realized several decades will have passed before there is any appreciable decrease in these percentages. Therefore discussion of neurosyphilis is still necessary.

Syphilis of the nervous system can be classified pathologically into meningeal, vascular and parenchymatous, according to the element of the nervous system most seriously involved. This classification is also of value in understanding the principles underlying treatment. It must be emphasized that these classifications are not mutually exclusive and that many cases show a mixture of two or all three types.

MENINGEAL NEUROSYPHILIS

It is safe to say that the meninges are primarily involved in all cases of neurosyphilis. The fact is of extreme importance, because this involvement can be recognized in the early stages of the disease by examination of the cerebrospinal fluid and proper treatment will prevent the spread of the infection to the blood vessels and parenchyma of the nervous system. Syphilis of the meninges may be subdivided into two groups, symptomatic and asymptomatic, according to whether signs or symptoms are present or the involvement is found only by examination of the cerebrospinal fluid.

Symptoms of involvement of the meninges may appear at any time after the infection,² but in

the vast majority of cases they appear within the first two years. These signs and symptoms are headache, stiff neck, mental confusion and cranial nerve palsies. Fortunately these signs and symptoms, with a few exceptions are of relatively minor import to the life or economic independence of the patient, and respond quite readily to treatment. Removal of the cerebrospinal fluid by lumbar puncture and routine treatment by an arsenical and bismuth will relieve the symptoms and most of the signs of the meningeal involvement within a few weeks. Unfortunately, this dramatic improvement often deceives the patient, and sometimes the physician into thinking that the disease is cured whereas in fact the battle has only just begun. Treatment must be continued for at least eighteen months, and longer if the cerebrospinal fluid is not entirely normal by the end of that time.

Symptomatic involvement of the meninges (syphilitic meningitis) is a relative rarity but either this or asymptomatic involvement (asymptomatic neurosyphilis) is always present before the development of parenchymatous neurosyphilis, and is only rarely absent in the cases that later develop signs of vascular neurosyphilis. It must be emphasized again that this fact is of extreme significance for the management of a patient with syphilis. The cerebrospinal fluid must be examined in every such patient. In primary or secondary syphilis this examination should be deferred until the patient has received treatment for a year to a year and a half since a negative finding in the early stage does not necessarily indicate that there will not be later involvement, and also positive findings in the early stages would not materially influence the method of treatment. On the other hand, the presence of a negative cerebrospinal fluid two or more years after the infection is almost absolute assurance that parenchymatous neurosyphilis will never develop, and a positive fluid at that stage is a serious warning of this danger, depending on the severity of the changes in the fluid³ and calls for continuation of therapy with or without modification until the fluid is entirely normal. In line with the above remarks, the cerebrospinal fluid should be examined immediately in all patients with latent syphilis two or more years after the infection or with signs or symptoms of tertiary syphilis of the skin, bones or viscera. The duration and mode of treatment

*Presented at the annual meeting of the New Hampshire Medical Society, Manchester, June 8, 1939.

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of such cases often depend on the results of this examination

The method of treatment of patients with asymptomatic involvement of the meninges varies somewhat in different clinics. Some authorities prefer to use tryparsamide immediately, but it is my practice to treat such patients with ten to twenty injections of neoarsphenamine (0.3 to 0.75 gm) at weekly intervals, followed by a similar number of injections of bismuth (1 or 2 cc) at weekly intervals. This alternation of courses is repeated until the cerebrospinal fluid is entirely normal. The cerebrospinal fluid is controlled by examination at intervals of four to eight months. Tryparsamide is substituted for the neoarsphenamine at the end of one year of treatment if there has not been a marked diminution in the severity of the alterations in the cerebrospinal fluid. Fever therapy is considered if the fluid shows little progress toward normality after another year of tryparsamide and bismuth therapy.

VASCULAR NEUROSYPHILIS

Signs or symptoms of involvement of the blood vessels of the brain or spinal cord may develop at any time after the infection. They are occasionally present at the same time as the early meningeal symptoms, but are commoner several or many years later. The signs of cerebral vascular neurosyphilis are similar to those found in arteriosclerotic disease of the cerebral vessels. Syphilis should be suspected whenever a young or middle-aged individual develops signs or symptoms indicating thrombosis of a cerebral vessel. The disease is quite probable if there is no evidence of hypertension or cardiorenal disease. The diagnosis is established by the results of blood tests and examination of the cerebrospinal fluid. It must be remembered that changes in the fluid may be of any degree of severity or be entirely absent, depending chiefly on the amount of accompanying syphilitic meningitis.

Syphilitic involvement of the blood vessels of the spinal cord usually produces varying degrees of spinal myelitis, with pains, spasticity and weakness of the legs, or a complete transverse myelitis with a flaccid paraplegia. Multiple sclerosis and spinal-cord neoplasms are usually considered in the differential diagnosis, and the diagnosis can only be made by examination of the cerebrospinal fluid.

The treatment of vascular neurosyphilis is the same as that outlined for meningeal neurosyphilis. Dramatic results cannot be expected. The most that can be accomplished is the clearing up of any inflammatory reaction. The degree of functional recovery depends to some extent on how

much of the symptomatology is produced by the inflammatory exudate, but mostly on the size and number of thrombosed vessels.

PARENCHYMATOUS NEUROSYPHILIS

Parenchymatous neurosyphilis usually takes the form of parietic or tabetic neurosyphilis. Other rarer forms are primary optic atrophy and chronic anterior poliomyelitis.

Paretic neurosyphilis (dementia paralytica, syphilitic meningoencephalitis) is the most serious form of syphilis of the nervous system. If untreated it leads inevitably to dementia and death, and it is not arrested in time, to partial dementia and economic dependence. The cardinal symptoms of this disease are changes in personality and evidences of mental deterioration. Convulsive seizures and transient focal neurologic signs are not uncommon. With progress, the disease may simulate any one of the known psychoses. Neurological examination of the patient often reveals only tremor of the mouth and tongue and hyperactive reflexes. The diagnosis is made on the appearance of signs and symptoms of organic mental disease and by results of examination of the cerebrospinal fluid, which always shows the characteristic abnormalities.

The results of treatment of paretic neurosyphilis with the arsphenamines and the heavy metals have been very disappointing, and it was not until the introduction of fever therapy by Wagner von Jauregg⁵ and tryparsamide by Jacobs and Heideberger⁶ that any progress was made in the treatment of this disease. With these newer methods, it can be arrested in over 50 per cent of cases, and more than 30 per cent of patients⁷ can be restored to their former station in society. The decision as to what mode of therapy—tryparsamide or fever—is to be used in a given case depends on the status of the patient at the time the diagnosis is made. If there are only mild personality changes or minor evidences of mental deterioration and the patient is able to continue his work, treatment with tryparsamide (1 to 3 gm at weekly intervals) can be tried. If there is no further progress of the disease, the treatment can be confined to tryparsamide. Two to five years of treatment are necessary, and occasional examinations of the spinal fluid are of value in estimating the progress of the treatment. If satisfactory progress is not being made in the arrest of the disease as manifested by increase in symptoms, the patient should be hospitalized and fever therapy given. Fever therapy is immediately indicated if the patient presents himself with moderate or marked mental deterioration and is unable to work.

The common modes of fever therapy in use in

this country are the induction of malarial fever by inoculation with malaria organisms and the artificial induction of fever by heat cabinets.⁸ There has been a great deal of argument as to the relative value of these two modes of therapy but the results are quite comparable and the choice depends on the facilities at hand. The heat cabinets are quite expensive and require a great deal of technical and nursing assistance, while malaria can be given to a patient in any general hospital. The mortality rates for the two forms of treatment are not appreciably different. Fever therapy should always be followed by treatment with trypanamide or one of the trivalent arsenicals for a period of two to five years depending on the clinical progress of the patient and the rapidity of the reversal of the spinal fluid to normal.

Tabetic neurosyphilis (tabes dorsalis) like parietic neurosyphilis, is a late manifestation of the disease. The symptoms usually develop five to thirty years after the initial lesion. The early symptoms are lightning pains in the extremities, difficulty in walking especially in the dark, and disturbance of the control of the urinary bladder. With progress of the disease there may be very marked ataxia and weakness of the lower extremities, atrophy of the optic nerves, other cranial nerve palsies, gastric and visceral crises, trophic ulcers and Charcot joints. Neurological examination of the patients shows a diminution or absence of the reflexes in the lower extremities, impaired vibratory and position sense in the legs, abnormal pupillary reactions⁹ and changes in the cerebrospinal fluid.

The treatment of tabetic neurosyphilis is poorly standardized in comparison to that of parietic neurosyphilis. Fortunately, the course of the former is benign in comparison to that of the latter leading to death only in rare cases, and not infrequently coming to a spontaneous arrest leaving residual scars in the form of absent reflexes, impaired pupillary reactions and a varied degree of ataxia, impaired bladder function or cranial nerve palsies. Good results can be obtained in some early cases by routine treatment with the trivalent arsenicals and bismuth. Better results are usually obtained by the use of trypanamide. Trypanamide, of course, cannot be given when there are signs or symptoms of involvement of the optic nerve. Failure to respond to the intravenous treatment indicates that fever therapy should be tried. This should be followed by

intravenous and intramuscular injections, as in the case of parietic neurosyphilis. The introduction of salvarsan serum intraspinally (Swift-Ellis treatment) which was in vogue several decades ago has waned in popularity, and has been replaced in practically all clinics by trypanamide or fever therapy.

The results of treatment of tabes dorsalis are not so dramatic as those obtained in the treatment of parietic neurosyphilis. Usually the progress of the disease can be arrested but the troublesome symptoms—gastric crises, lightning pains and so forth—may continue. Also the results of the treatment of the optic atrophy of tabes dorsalis and the primary optic atrophy of syphilis are disappointing. All forms of treatment have been tried in such patients, but good results are reported in only a small percentage. Trypanamide is contraindicated and if the progress of the atrophy is not interrupted by routine treatment with neosphenamine and bismuth fever therapy should be used.

SUMMARY

Involvement of the nervous system can and should be prevented by the prompt and adequate treatment of primary and secondary syphilis. Serious damage to the nervous system can be prevented by the energetic treatment of patients with symptomatic or asymptomatic evidence of involvement of the meninges.

The therapeutic agents of value in neurosyphilis are those used in the treatment of syphilis elsewhere in the body with the addition of pentavalent arsenicals (trypanamide) and fever therapy. The duration of treatment of neurosyphilis is not measured in weeks but in months and years.

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REPORT ON MEDICAL PROGRESS

DISEASES OF THE THYROID GLAND

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IT HAS been requested that the authors of these reviews be selective and critical rather than comprehensive in the treatment of their subjects, also that they stress the practical rather than the theoretical, the former being presumably of more interest to practitioners. I shall attempt to abide by this request in so far as seems reasonable. I cannot, however, refrain from submitting that sound practice is usually the fruit of sound theory, and that if the practitioner is not interested in the scientific basis of his art, he ought to be. As a matter of fact, I believe that the practitioner is interested in scientific groundwork, and shall therefore have something to say about it in what follows. Indeed, did I not do this there would not be much material for review, because no evidence has been found that significant advances have been made during the last year in the diagnosis and treatment of diseases of the thyroid gland.

The surgery of the thyroid, for example, which has already reached a high degree of perfection, has not significantly altered, even in the last several years, except in so far as gradual improvement in the evaluation of operability of patients and in the niceties of preoperative and postoperative care, anesthesia and operative technic has reduced mortality and postoperative complications. What can be accomplished along these lines in the case of toxic goiter is excellently set forth in the papers of Sir Alan Newton,^{1,2} to which the reader is referred. So perfect, indeed, has thyroid surgery become that it seems that it has almost reached its limit, and that further progress in the therapeutics of thyroid diseases will be along lines other than surgical.

Endocrinological research, by contrast, has been almost hectically active, so much so, in fact, that it is almost impossible to keep up to date on its progress. Of course, many results are incomplete and experiments poorly conceived or controlled, yet out of the mass of material produced it is possible to draw certain new conceptions of the morbid physiology of the thyroid gland which are bound sometime, if not immediately, to alter our methods of diagnosis and treatment of its diseases. A huge literature is accumulating, for example,

on the thyrotropic hormone produced by the anterior lobe of the pituitary. The appearance of this principle on the endocrinological scene has, among other things, revived active interest in the etiology of Graves's disease. Indeed, in considering these days, any disease of the thyroid gland which involves a disturbance in its function, orientation can perhaps be best achieved by thinking in terms of three substances and their physiologic actions and interactions, these being the thyroid hormone, the pituitary's thyrotropic hormone and the element iodine. That the pituitary's thyrotropic, or thyroid-stimulating, hormone regularly causes increased secretory activity of the thyroid gland, manifested morphologically by changes in the direction of hyperplasia and functionally by increased metabolic rate and other speed-ups characteristic of the action of thyroid hormone, is now well established. There is also evidence, though as yet less weighty, that the thyroid hormone exercises an inhibitory influence on the thyrotropic function of the anterior lobe of the pituitary (Aron,³ Aron et al.,⁴ Kuschinsky,⁵ Marine^{6,7} and Gessler⁸). Should this evidence eventually prove correct, there emerges a functional equilibrium between two glands achieved by means of two hormones, one made by each gland and acting through its concentration in the blood on the other. The factors influencing such an equilibrium are obviously many: the rate of fixation, the destruction or excretion of the hormones, the development of antihormones and the action of neurogenic or humoral agents other than the hormones themselves on their rate of manufacture.

If we recall that Graves's disease is often precipitated by a psychic trauma, the question of whether either the thyroid or pituitary gland can be stimulated or inhibited in its secretory function directly through nervous pathways becomes of practical importance. Although it is well known that the thyroid gland has a rich innervation, the weight of evidence at the present time favors the view that this is not directly secretory, but rather vasomotor, and that secretory activity of the thyroid gland is not governed directly through nervous channels, but only humorally (Nonidez,^{9,10} Cahane and Cahane¹¹ and Uotila¹²). On the

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other hand, evidence is accumulating that the secretory activity of the pituitary gland can be influenced directly through nervous channels (Friedgood and Pincus¹²), and even that there are centers in the midbrain which control thyroid function via the anterior pituitary gland, the hook up thus being first nervous, then humoral (Fenz¹³ and Cahane and Cahane¹¹)

These neurohormonal relations bear significantly on the etiology and pathogenesis not only of Graves's disease but also of myxedema. With the emergence of the pituitary's thyrotropic hormone, the question at once arises concerning both these diseases, Is the pituitary gland more to blame than the thyroid gland? In the case of Graves's disease certain writers, notably Marine,⁶ early seized on the theory that this disease results from hyperfunction of the anterior lobe of the pituitary with respect to thyrotropic hormone. Others, such as Fellingner,¹⁶ Spence,¹⁶ Cope¹⁷ and myself hold to the view that at least ordinary Graves's disease is not caused primarily by hyperfunction of the anterior pituitary. It is possible as Spence admits, that there are certain cases primarily pituitary in origin and a larger group in which the thyroid hyperfunction is occasioned by some other mechanism. When a picture of Graves's disease is encountered as part of acromegaly, it seems reasonable to suppose that it is due primarily to anterior lobe hyperfunction. Important as is the question of which gland is chiefly at fault, it cannot at present be answered with finality because of the lack of satisfactory methods of study. The titers of the two hormones in the blood, if they could be determined accurately, might provide a solution of the problem, but as yet neither of them can be. Blood iodine determinations can be made, to be sure, but there is great uncertainty (Salter¹⁸) concerning what fraction of total iodine represents hormone iodine, and indeed it is unknown in what form the hormone is carried in the blood stream. Lerman's¹⁹ work suggests that it is not carried in the form of thyroglobulin because with a serum immune to thyroglobulin he can detect no appreciable amount of that protein in the serum either of normal persons or of thyrotoxic or myxedematous subjects. Nor is he able to detect any thyroglobulin in human urine. It is highly interesting, although perhaps not as yet clarifying that Salter and Lerman¹⁸ were able to relieve myxedema completely with an iodinated indifferent protein such as serum albumin. Evidently the thyroidless individual is able to derive active hormone from such material. This fact increases the difficulty of interpreting blood iodine values, and more than that it may necessitate a complete reconstruction of our theory

of the role of the thyroid gland in the manufacture of what has been called the thyroid hormone. Perchance instead of being the factory of the hormone, the gland is no more than its distributing warehouse.

When it comes to thyrotropic hormone the difficulties are still greater, because no chemical approach is available. Determination of thyrotropic activity of the material under investigation, by observation of its effect on the thyroid of a test animal is all that is possible. This is called bioassay. It has the limitation that it discloses only the net amount of thyrotropic activity present—that is to say, the amount of thyrotropic activity over and above whatever antithyrotropic activity may be present. Nevertheless, a rapidly increasing number of bioassays for thyrotropic hormone in clinical cases are appearing in the literature (Aron et al.,⁴ Krogh and Okkels,²¹ Hertz and Oastler,²² Fellingner,¹⁶ Spence,¹⁶ Emerson and Cutting,²³ Cope,²⁴ Starr et al.²⁴ and Jones²⁵) and while there is much conflicting data, the results tend to show that there is less thyrotropic activity in the blood and urine of thyrotropic persons than in normal subjects, and rather more in that of persons who have been cured of thyrotoxicosis by subtotal thyroidectomy. Hertz and Oastler, using pituitarectomized rats as test objects, have found increased thyrotropic activity in the serum and urine of myxedematous patients. This has been partially confirmed by Starr et al., using intact guinea pigs as test objects.

In the recent literature there are also to be found numerous other types of investigations on thyrotropic hormone and antithyrotropic agents, and other factors which may influence the thyroid gland humorally. Thus, it has been shown that thyrotropic hormone selectively increases the metabolism of isolated thyroid tissue (Paal,²⁷ Anderson and Alt²⁸ and Canzanelli and Rapoport²⁹), and Williams³⁰ has shown that the secretory cycle of thyroid follicles, which he observed directly in autografts in the rabbit's ear are accelerated by giving the animal material possessing thyrotropic activity. What seems a singularly important piece of work is that of Foot, Baker and Carrel,³¹ in which human thyroid glands removed at operation were cultivated in toto in the Landbergh apparatus. The significant result thus obtained was that the histological picture reached by the gland under such circumstances seemed determined, not by the phase of activity which had pertained while it resided in the body to which it belonged but by the nature of the perfusate used during its existence in vitro. A possible implication of such findings is that in Graves's disease the

state of hyperplasia of the thyroid gland is the consequence of predominantly thyrotropic properties of the blood that reaches the gland, rather than that of any condition inherent in the gland itself. From the practical side, however, it can be said that in the patient the only agent which we as yet have by which, in Graves's disease, the thyroid gland can be beneficially affected humorally is iodine, and that our chief attack must still be aimed directly at the thyroid gland in the form of surgical resection or irradiation.

The mode of action of iodine in toxic goiter is still a matter of debate. My colleagues and I (Means and Lerman³² and Means³³) believe that its action is directly on the thyroid cells, whose function it alters by a blockade of some sort, leading to increased storage of hormone in the gland and decreased delivery to the body. Eason,³⁴ however, submits that there is no evidence that iodine acts directly on the thyroid cells, and there are some who believe that it acts primarily on the pituitary gland or even on the midbrain. One thing is clear, however: it does not act on circulating thyroid hormone. Giving iodine has no effect on thyrotoxicosis produced by the administration of thyroid extract.

Because of the essential role of iodine in thyroid economy, iodine tolerance tests of various sorts are rapidly making their appearance, designed both for investigative and for diagnostic purposes (Elmer,³⁵ Perkin, Brown and Lang,³⁶ Watson^{37, 38} and Litchfield³⁹). While these tests are yielding information of interest, the difficulties of interpretation of the significance of variously bound fractions of iodine in the blood stream, and the variance of results obtained by different methods, make me believe that not yet has this type of observation become of great diagnostic importance.

While we are on the subject of iodine, mention should be made of a new type of investigation of thyroid problems which depend on the use of iodine rendered radio-active, the course of which through the animal body, can be traced by virtue of its radio-activity. Hertz, Roberts, Means and Evans,^{40, 41} in Boston, and Hamilton and Soley,⁴² in San Francisco, have reported observations of this type. In animals it has been shown by the former that the thyroid gland traps iodine very rapidly and quickly becomes saturated with it. In certain types of hyperplasia of the thyroid gland, although the collection of iodine by the gland is greater than in normal conditions, the threshold for iodine uptake seems elevated. That is to say, certain hyperplastic glands are less able to utilize small quantities of iodine than are normal glands, but have the capacity of taking

up more iodine from large doses. This may throw further light on the mechanism of Graves's disease, in that it explains how a gland known to have a great affinity for iodine still does not cure itself by taking up the small quantities of iodine normally found in the diet, but can be definitely benefited by the administration of relatively large amounts of iodine. Hertz and Roberts have also administered radio-active iodine to human subjects with goiter, and when the thyroid gland has been removed at operation, determined the amount collected by the gland and its chemical combination.

The hormonal pattern in myxedema is perhaps somewhat easier to visualize than is that of Graves's disease. Here again the possibility of a pituitary variety (hypofunction of the anterior lobe with respect to thyrotropic hormone) and a primary thyroid variety presents itself. The weight of evidence, as in Graves's disease, points strongly away from the pituitary gland in the usual case of myxedema. A primary thyroid atrophy seems to be the cause of classic myxedema, and the hormonal set-up a simple shortage of one hormone, that of the thyroid gland. It is becoming apparent, however, that there are exceptional cases (one has been reported by Castleman and Hertz,⁴³ and several others have been seen in my clinic) in which thyroid hypoplasia with a resulting picture of myxedema is secondary to lack of anterior lobe function. These cases may be indistinguishable at first sight from ordinary myxedema, although the presence of amenorrhea in place of the usual menorrhagia of myxedema is highly suggestive of a pituitary origin. The practical importance of the group is that on thyroid therapy they may do badly, may in fact go into a state of shock similar to that seen in Addison's disease, and due, indeed, to the aggravation of a subclinical hypocortinism of pituitary origin by the administered thyroid, quite analogous to the aggravation of diabetes seen in persons with both myxedema and diabetes when thyroid is administered. The point of practical importance is that it behooves the physician to study the hormonal signs in his patients which seem to be myxedematous, and in inaugurating thyroid therapy to proceed with caution and have the patient under close surveillance. When the type of reaction mentioned above is observed, it may be necessary to protect the patient with a high salt diet and possibly cortin while administering thyroid, and the gonadotropic hormone of the anterior pituitary gland may be desirable as well.

In the older literature one finds accounts of the co-existence of myxedema and Graves's disease. Of course, it is impossible to have both too much

and too little thyroid hormone produced at the same time nevertheless, it is possible for certain manifestations of Graves' disease, for example the eye signs, to be present at a time when the patient is unmistakably on the hypothyroid side, as for instance occasionally after extensive subtotal thyroidectomy. This fact leads naturally to a related one, namely that in certain cases of Graves' disease the eye signs seem to become quite divorced from the thyrotoxic signs, and to vary independently as though of different causation. In a patient with no discoverable clinical signs of thyrotoxicosis one may see eye signs of marked degree, or in a patient originally thyrotoxic with slight eye signs one may observe progressive and serious exophthalmos after thyrotoxicosis has been completely abolished by thyroidectomy (Thomas and Woods⁴⁴ and Ginsburg⁴⁵). One may even see marked eye signs in persons frankly myxedematous. Brain⁴⁶ has described the former picture under the title of "exophthalmic ophthalmoplegia," a not altogether satisfactory term because cases are not infrequently found evidently of the same general nature as those described by him, in which there is no ophthalmoplegia. The clinical importance of this special subgroup of cases of Graves' disease is that in them the safeguarding of the eyes may be the major problem. In the more malignant types the orbital decompression operation of Naffziger⁴⁷ may become necessary, but in many others the condition is fortunately less serious. Some evidence is accumulating that the administration of thyroid benefits the eye condition in some of these cases. Especially if the basal metabolic rate is low thyroid can be tried quite freely. A possible theoretical explanation of a beneficial action of thyroid on the eyes under such circumstances would be that the eye signs are due to pituitary hyperfunction as Marine⁷ contends, and that thyroid inhibits the pituitary gland. When the basal metabolic rate is not below normal, good results have sometimes followed the combined use of thyroid and iodine. The iodine by direct action on the thyroid gland holds the basal metabolic rate at a lower level than would obtain in its absence, and this gives more opportunity to exhibit thyroid hormone without producing alimentary thyrotoxicosis. Whether this reasoning is sound is far from certain but it is true that a number of patients have shown improvement under such combined treatment. Good results have also been claimed for irradiation of the orbit or the pituitary gland (Ginsburg⁴⁵).

The relation of thyroid function to gonadal function has of late attracted much attention from both biological and clinical investigators. The thy-

roid hormone unquestionably affects all other endocrine glands, at least to the extent of accelerating the rate of metabolism of their cells as it does that of all cells. This might be called a non specific effect. Whether the thyroid hormone acts on other glands more specifically—we have already indicated that it may inhibit certain functions of the anterior lobe of the pituitary gland—is a question of both theoretical and practical importance. To the various speed ups characteristic of thyroid hormone action can now be added the increased rate of egg laying by hens receiving thyroid hormone (Wiochester⁴⁸) and of milk production by cows (Graham⁴⁹). Whether these effects, which incidentally may be of the non-specific variety, constitute good news for dairy and poultry farmers, or whether the ill effects of thyroid feeding offset the increased yield, I am not competent to say. Perhaps those physicians who engage in gentleman farming for their release may answer the questions. That thyroid feeding renders certain sterile women fertile and enables certain habitual aborters to go through normal pregnancy has long been known (King and Herring⁵¹). Also long known in the field of thyro-ovarian relations are the menstrual patterns in myxedema (characteristically menorrhagia) and in thyrotoxicosis (characteristically oligorrhea or amenorrhea). Good results are reported in the treatment of various menstrual irregularities by thyroid (Foster and Thornton¹). All these may also belong in the realm of non specific action. More recently, however there has been accumulating evidence of more specific effects. For example, Tyndale and Levin⁵² found that the stimulation of ovarian follicles which ordinarily occurs when menopausal urine is injected into immature hypophysectomized rats was markedly decreased by the simultaneous injection of thyroxine. They concluded that the thyroid hormone exerts an inhibiting action on gonad stimulation which is a direct one and not mediated through the pituitary gland since it was demonstrated in pituitarectomized animals. Membrives⁵⁴ on the other hand, reports that the ability of implants of the anterior pituitary gland to cause ovarian development and consequent vaginal canalization in immature rats was increased by thyroid feeding and decreased by thyroidectomy. This may be a non specific effect in contrast to that observed by Tyndale and Levin which would appear to be specific. It is of interest, furthermore, that Gessler⁵⁵ has shown that the ovarian hormone, folliculin (estron) has the power to lower the basal metabolic rate of normal guinea pigs and that of hypophysectomized rats, a power which he attributes to an antithyroid property. Of course such observations as these are fragmentary and

their medical significance is obscure, yet they are not without practical interest, for they may indicate a new approach, the hormonal, to the treatment of thyrotoxicosis. Indeed, Starr and Patton^{56, 57} have already shown that remissions can be produced in hyperthyroidism by treatment with an extract of pregnancy urine. They do not undertake to explain the mechanism, but it seems fair to consider it related to the experimental results cited above, and perhaps due to a thyro-inhibitory action of estrin which the gonadotropic activity of pregnancy urine would cause to be secreted in increased quantity.

A quite different indication of balance, or dependence, of function between the thyroid gland and gonads is to be found in the age and sex incidence of thyroid diseases. A recent paper by Bram⁵⁸ gives some interesting data. In children he finds the incidence of exophthalmic goiter is 1 boy to 20 girls, in young adults 1 man to 5 women and in elderly persons 1 man to 2 women.

Geographic incidence may also throw light on etiology. In the case of exophthalmic goiter such information has long been wanting. Now, however, Read⁵⁹ has supplied it. His studies disclose that the distribution of exophthalmic goiter, that is to say the morbidity of this disease, is far more uniform throughout the United States than is that of endemic goiter. This finding is strong evidence that the two diseases are etiologically unrelated. With regard to the etiology of endemic goiter, Kimball⁶⁰ claims that twenty years' experience with goiter prophylaxis proves that this disease is one purely of iodine deficiency, and preventable. The best method of prophylaxis is by iodized salt, and in preventing endemic goiter, according to Kimball, adenomas, toxic goiters, cretinism and deaf mutism are likewise prevented. In so far as Kimball's contention applies to exophthalmic goiter, I must dissent. The work of Read, cited above, seems to me to refute this portion of Kimball's argument. Nonetheless, goiter prophylaxis is one of the triumphs of modern medicine, and not only originated in the United States but has been conducted most successfully here. For example, Kimball points out that in Switzerland, where the iodized salt is poorer in iodine than that used in this country, the results have been less impressive.

The recent literature indicates considerable interest in the results of treatment of cretinism. Some writers are more optimistic than others. Most stress the importance of early diagnosis and thorough treatment. Lewis, Samuel and Galoway⁶¹ claim that cretins can become mentally normal on treatment. They, however, point out that promptness and continuity of treatment are not the sole factors determining the degree of men-

tal recovery. Other factors are degree of development at the time that symptoms appeared, cerebral damage at birth and hereditary endowment. That is to say, thyroid administration will not make the cretin any better mentally than he would have been had he not been a cretin. Brown, Bronstein and Kraines,⁶² while admitting that early recognition and persistence in treatment are very important, find that even when these are achieved the majority of patients fail to attain normal mental growth. The chances, so these authors claim, that at maturity the mental age will be more than ten or eleven are not great. The curves of mental growth in treated cretins are of the same general shape as those in normal children, but lie at a lower level.

In this connection it is pertinent to note that thyroid hormone is in a sense a growth hormone. Not alone in cretins, but in certain pituitary dwarfs also, it promotes growth in a very satisfactory manner. On the experimental side Evans, Simpson and Pencharz⁶³ have shown that growth promotion secured by anterior pituitary extracts, although not dependent on the presence of the thyroid gland, is greater when it is present. Thyroxine, which promotes the growth of thyroidectomized animals, does not have this effect when administered to thyroidectomized pituitarectomized animals. A synergism exists between the anterior pituitary growth hormone and the thyroid hormone, which is independent of the anterior pituitary thyrotropic hormone.

In the non-endocrine, or perhaps better non-hormonal, varieties of thyroid disease, as for example cancer, inflammations and anomalies, I have found no contributions within the year sufficiently significant to rate mention in a review so restricted in length as is this one.

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A motion was made by Dr Butties that the report of the Nominating Committee stay on the table until the question of the constitution was decided. This was seconded and so passed.

President Lawliss appointed the following as members of the committee to report on the Medical Practice Act

Dr Farmer moved that the old constitution be revoked but that it should stay in effect until the new constitution was adopted. The motion was seconded and carried.

Dr Soule moved to have the new constitution adopted as presented by the committee which drafted it, with the exception of an amendment to Section 1, Paragraph 2, as follows: "That at the annual meeting a president, president-elect, vice-president, secretary, treasurer and auditor shall be elected." Dr H L Frost seconded this motion, and it was so voted.

Dr C C Shaw moved that the Resolutions Committee arrange a resolution to be presented at the afternoon meeting, extending greetings from the House of Delegates to the new dean of the University, Dr H A Kemp. This motion was seconded and passed.

Dr Frost moved that the report of the Nominating Committee be accepted. The motion was seconded and officers elected as reported by the committee.

Dr E J Quinn moved that the meeting be adjourned. The motion was seconded and carried.

CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTHEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACT B MALLORY, M.D., Editor

CASE 25471

PRESENTATION OF CASE

First Admission A sixty-three year-old chief of police was admitted to the hospital complaining of indigestion

The patient was well until three years before admission when he began to have indigestion described as a "hollow feeling" in the stomach. This was accompanied by gaseous, sour eructations, was worse at night, and was often relieved by soda. His family physician prescribed crackers and milk between meals and at bed time. He was relieved of his distress until three months before entry when he noted a return of sour eructations with vague epigastric distress, which was relieved by vomiting. On one occasion he vomited food eaten "one week before," but usually the food was that ingested one or two meals earlier, once he noted that the vomitus was blood tinged. These symptoms increased steadily. His bowels were regular with mineral oil, which he took nightly. He had felt poorly for three years and had lost 25 pounds in weight, the loss of 15 of which had occurred in the past year. The family, marital and past histories were noncontributory.

The physical examination revealed a well developed man who showed evidence of recent weight loss. The skin was dry and loose. The heart and lungs were essentially negative. There was an indefinite non tender mass palpable just beneath the right costochondral junction. The remaining examination was negative.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. The blood showed a red-cell count of 4,500,000 with 90 per cent hemoglobin, and a white-cell count of 10,300 with 65 per cent polymorphonuclears. A gastric analysis revealed a fasting free acid level of 28 units, with second and third specimens reading 30 and 41. All gastric and stool guaiac tests were negative. The blood Hinton test was negative. The serum protein was 4.8 gm per 100 cc., two weeks later it was 7.0 gm, the serum nonprotein nitrogen and chlorides were normal.

A gastrointestinal series showed a dilated stomach containing a considerable quantity of secretions and small particles of food. Peristalsis was

intermittent, sometimes reversed, and the waves were rather weak. No barium passed through the pylorus during fluoroscopic examination. The antrum of the stomach was irregular, and the visible portion of the duodenum was deformed. Re-examination seventeen days later showed a normal esophagus. The stomach was dilated and contained a small quantity of fluid. Barium passed the pylorus with great difficulty in spite of much hyperperistaltic activity of the stomach. There was a 2-cm. area of ulceration on the lesser curvature in the region of the pyloric valve. This crater lay both on the gastric and duodenal sides, slightly more on the latter. The base of the cap was deformed, the apex and second portions were normal. At the end of six hours there was a 50 per cent residue in the stomach, at the end of twenty four hours, a 10 per cent residue. A gastroscopic examination three days after admission showed that peristalsis was absent. The antrum was well seen down to what appeared to be pylorus, which remained slightly patulous throughout the examination. A small area along the lesser curvature near the pylorus could not be visualized due to angulation. The mucosa throughout was partially covered with adherent barium, but this did not interfere with the diagnosis of any gross lesion. The mucosa showed increased reddening but there was no verrucous appearance.

The patient ran an essentially uneventful hospital course for nineteen days, after which he was discharged to await further x-ray studies. His symptoms failed to improve on a medical regimen consisting of six feedings a bland diet, rest, frequent gastric lavage, belladonna and sedation.

Second Admission (two weeks later) At this time an x-ray examination revealed that the degree of pyloric obstruction had increased markedly. The stomach was grossly dilated and atonic, and no barium passed the pylorus during the forty five minutes of fluoroscopic observation. The area of ulceration involving the pyloric valve and prepyloric area was unchanged.

On the day after admission an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. LANGDON PARSONS Although there are a good many details lacking in the history, I think it is fair to assume that this man had an ulcer with a history extending back over a period of three years. The diet of milk and crackers prescribed by his physician gave moderate relief, but it is noted that he still felt poorly during the three year period. His symptoms became increasingly severe to the point where obstructive symptoms appeared a fact which I believe, brought

him to the hospital. There had been a moderate amount of vomiting, confirming the suggestion of obstruction. A definite change had occurred in the character of his symptoms. On physical examination we note weight loss, most of which had occurred during the past year. He may have been afraid to eat. The fact that he had the low serum protein responding rapidly to treatment suggests that a dietary factor was involved, possibly merely an inadequate food intake over this period. Despite the history of vomiting there is no evidence of dehydration, and it was evidently not of sufficient severity to affect the level of the nonprotein nitrogen or chlorides. There was no hematemesis, although he did have a little blood-tinged vomitus in one episode. The blood picture was normal, and negative guaiac tests were found not only on the gastric contents but also on the stools. The patient, therefore, had no bleeding from his lesion, which we presume was in the upper gastrointestinal tract.

There are two positive findings: the presence of an indefinite mass and the moderately high acid obtained on gastric analysis. The mass is described as indefinite. It is rather hard to evaluate a mass in this particular locality. A suggestion of an indefinite mass in the epigastrium is often difficult to confirm on subsequent exploration. This finding is of no great significance then except for the fact that the so-called mass was nontender. Thus we are left with a history suggesting ulcer and a moderately high acid discovered on gastric analysis. Our next help comes from the gastrointestinal series where the first examination revealed obvious obstruction at the pylorus, an irregular antrum and a deformed duodenum.

DR AUBREY O HAMPTON: This is the film of the stomach on the first examination, and this is one on the second. Obviously the stomach was grossly dilated at both examinations—more on the second. The character of the defect in the antrum is probably significant. It is not a smooth round curve as you would expect it to be if this ulcer were in the duodenum or at the pyloric valve. The ulcer is apparently in the cavity of the antrum on both examinations. If the barium was made to flow away from the antrum then the ulcer was visible in that area. The ulcer was larger than is stated in the record. I should think it was nearly 2 cm in diameter rather than 4 mm.

DR PARSONS: It makes a good deal of difference to me whether it is in the pyloric ring or the prepyloric area.

DR HAMPTON: We were sure the ulcer involved the stomach. It may have extended into the pyloric valve. This film was taken seventeen days later, and if anything the ulcer is larger.

DR PARSONS: Seventeen days later further x-rays revealed the same obstruction of the pylorus, an irregular antrum and a deformed duodenum. A 50-per-cent residue was noted in six hours, and a 10-per-cent residue in twenty-four. Hyperactive peristalsis was observed. A 2-cm ulcer was seen which may have arisen at the pyloric valve or on the gastric side. The crater, however, lay both on the gastric and the duodenal sides of the pylorus. A gastroscopy was done which was chiefly interesting because of what it did not show rather than because of what it did show. There was no evidence of gastritis except for the reddening of the gastric mucosa, and the observer failed to see any lesion of appreciable size or in fact any lesion. One thing I should like to ask Dr Benedict is why the pylorus was patulous at the time of gastroscopy. There was 50-per-cent residue and nothing seen going through at the time of the fluoroscopic examination and the gastrointestinal series.

DR EDWARD B BENEDICT: What was seen may not have been the pylorus, it may have been the prepyloric wave that sometimes appears.

DR PARSONS: We are dealing with an ulcer which gave symptoms of obvious obstruction—either a duodenal ulcer encroaching on the pylorus, a peptic ulcer occurring at the ring or a prepyloric ulcer. If it was a prepyloric ulcer, was it benign or malignant?

I think we can work up a fairly good history for ulcer. He had a three-year history of symptoms which is certainly suggestive. There was at least partial relief of these symptoms on a medical regime, although the process finally went on to the point of obstruction. The patient doubtless did not adhere any too rigidly to his medical diet. He was a chief of police, and it was stated that he was on a milk and cracker diet. I can conceive of several breaks occurring in such a diet in a patient with that occupation. There was no evidence of anemia. A high acid was found on gastric analysis. There was failure to see the lesion on gastroscopy. The ulceration appeared to extend through the pyloric ring and to involve the duodenum. Finally the patient was discharged from the medical service on an ulcer regime. These are all facts which build up a good case for ulcer, but do they necessarily mean that this patient did not have carcinoma?

First, take the three-year history. I have recently been reviewing the cases of carcinoma of the stomach in this hospital. From the point of view of history the patients can readily be divided into two groups: those who had symptoms for six months and those whose story extended over 2 years. Of patients who came to gastric resection,

5 per cent of those who had symptoms for six months were alive after five years and 35 per cent of those with symptoms of over a year were alive after the same period. The history does not rule out carcinoma. The weight loss possibly bears out the diagnosis of cancer although it may have been due to an inadequate food intake. The blood was normal. It is possible to have normal blood with carcinoma of the stomach and it is rare to find a red-cell count below 3,000,000 or a hemoglobin below 50 per cent. Not all gastric carcinoma patients bleed and we find that there were negative guaiac tests on the stools. In itself high acid does not necessarily point toward ulcer; we find you can have a high acid in cancer particularly when the lesion arises in the pyloric area. About 18 per cent of the group of gastric cancer patients had either a normal or a high acid. The most puzzling observation is the fact that this ulceration extended over into the duodenum. At one time we were taught that carcinoma of the stomach did not invade the duodenum but we now know this is not the case for we have seen it extend as far as 3 cm. on the duodenal side when the primary lesion was in the stomach. So this fact does not rule out carcinoma of the stomach. Did the ulceration occur in the pyloric ring? We have come to regard prepyloric ulcer as cancerous until proved otherwise, but we cannot say the same thing for ulceration occurring in the pyloric valve. No evidence of gastritis was seen on gastroscopy. I believe you would find some evidence of gastritis other than reddening of the mucosa if this were a duodenal ulcer. This is not always true, but I should be rather surprised not to find it.

DR. BENEDICT: There was some superficial evidence of gastritis. I intended my description to indicate that.

DR. PARSONS: Finally, no improvement was noted in this patient, either by x-ray or clinically after his discharge from the hospital on a medical regime. I grant that he returned only two weeks after he had left the hospital; no improvement was noted however.

I am inclined to think that this patient was operated on for an obstructing ulcer but I believe that the serial sections of the ulcer will show cancer, possibly a carcinoma in situ. If so it was probably carcinoma in situ from the beginning thus accounting for the long history. At any rate I believe this patient had an ulcerating carcinoma of the stomach. If the lesion was found to be confined to the stomach he had a 62-per-cent chance of living five years.

DR. CHESTER M. JONES: I am sorry Dr. Leland McKittick is not here. I saw this patient with

him, and we went through the same line of reasoning as Dr. Parsons has just outlined. My feeling after we had seen him for a day or two was that we had to consider the diagnosis of cancer and I wrote down on the discharge note. X-ray studies show a big pyloric lesion and twenty-four hour stasis. In the absence of pain I am anxious about the diagnosis. I think he will come to operation, and I am a little fearful of cancer. He is to go home for a short time and return for further x-ray studies in two weeks. I did not feel justified in letting him go home except with the stipulation that he return in a short time, he was allowed to go only because of his request.

Another thing to point out is the question of pyloric obstruction. The roentgenologists frequently make a diagnosis of pyloric obstruction only to find a few days later there is no stasis whatever. He had frequent gastric lavages, and the amounts removed by gastric aspiration on March 10, 11, 12, 15 and 22 were 240 cc., 240 cc., 30 cc., 180 cc. and 120 cc. respectively. This proves that the stasis was transient, and the actual diagnosis of pyloric obstruction should have been made with a certain amount of reservation. The fact that the stomach was large is in favor of there having been more or less obstruction for quite some time. On reentry he reported that he had had no pain and had only vomited once in two weeks, x-ray study showed about the same findings as before. We decided the only thing to do was to operate, with the expectation of finding an ulcer and quite probably a cancer. Dr. McKittick operated on that basis.

DR. J. H. MEANS: How much credence do you give to the statement that this patient vomited food eaten one week before?

DR. JONES: All I can say is that this man had a one-track mind and insisted that it was a correct statement. He was so fearful of discomfort that he had been cutting down his diet for weeks before he came in and had a low serum protein because of it.

DR. MEANS: If he had such good acid in his stomach I do not believe any food would be recognizable after a week's interval. I draw the conclusion he must have been mistaken.

DR. TRACY B. MALLORY: I should like to ask Dr. Benedict what other evidence of gastritis he would expect to see in a case with a widely dilated stomach other than reddening of the mucosa. Could you expect hypertrophied rugae in such a stomach?

DR. BENEDICT: No, but gastroscopic evidence of gastritis does not depend on hypertrophy alone. It is based on a verrucous appearance which was not present in this case.

DR. JONES: Coming back to the question of x-ray

sis, I might add that there were two drops of mucus reported by Dr Benedict at the preliminary drainage

PREOPERATIVE DIAGNOSIS

Prepyloric ulcer?
Carcinoma of the stomach with obstruction?

DR. PARSONS'S DIAGNOSIS

Carcinoma of the stomach

ANATOMICAL DIAGNOSIS

Carcinoma of the pylorus and prepyloric region

PATHOLOGICAL DISCUSSION

DR MALLORY This patient was operated on by Dr McKittrick who found a readily palpable mass in the region of the pylorus and, without hesitation, did a subtotal gastrectomy. After the specimen was opened a lesion about 2.5 cm in length and 1 cm in depth was found which occupied part of the pylorus and prepyloric region. In which area it started I cannot say. There was a fairly deep ulcer crater in the center, and the induration extended through all the layers of the wall even the serosa. On microscopic examination we found frank carcinoma with, I should say, quite typical peptic ulceration in the center of the cancer. It is a very common thing to find true peptic ulceration in a malignant lesion and for that reason among others it is not surprising that the symptomatology may be very confusing.

CASE 25472

PRESENTATION OF CASE

A forty-year-old Italian truck driver was admitted complaining of periodic pain in the epigastrium.

Thirteen years before admission the patient complained of anorexia, vomiting and pain in the epigastrium. He was treated by an outside physician with a diet and "powders" which "cured" him in one year. He apparently lost and regained some 50 pounds in weight during this time. X-ray films of the stomach taken some time during this illness were reported as negative, and he subsequently experienced only occasional "gas pains." He was able to drink beer and wine and eat well, and he had no trouble similar to the first attack until four years before entry when on one occasion he vomited coffee-grounds material. He remained in bed for two weeks and had no further known symptoms until six months before admission when vomiting, anorexia and epigastric pain again appeared. The pain sometimes radiated to the lower

part of the sternum or through to the mid-back, usually developed three to four hours after meals or at night and was relieved by soda, by vomiting or by the ingestion of milk. He frequently vomited about fifteen minutes after eating a meal, the vomitus consisting of ingested food without blood. He was gradually forced to stop taking solid foods, and his weight had dropped 30 to 40 pounds during the six months before admission. He had passed no tarry stools.

The past, family and marital histories were not contributory.

The physical examination revealed a muscular, well-developed man who showed slight evidence of recent weight loss. The findings were essentially negative except for the presence of subjective pain, without tenderness or spasm, located at a point in the mid-epigastrium between the xiphoid and umbilicus. The blood pressure was 120 systolic, 78 diastolic.

The temperature, pulse and respirations were normal.

The examination of the urine was negative, and that of the blood showed a red-cell count of 5,300,000 with 92 per cent hemoglobin, and a white cell count of 10,700 with 64 per cent polymorphonuclears. On admission the stools were yellow, soft and formed and showed a +++ guaiac test. Another stool examination the day before operation was guaiac negative. A serum protein was 6.6 gm per 100 cc. X-ray studies of the chest were negative. A gastrointestinal series showed in the immediate prepyloric region a constant narrowing with spasm. There was an irregular ulcer crater 4 to 5 mm in size in the pylorus, if anything slightly on the prepyloric side. There was convergence of the rugae toward the ulcer, but no evidence of surrounding infiltration.

On the fifth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR EDWARD B BENEDICT Here we have, as I see it, the problem of an ulcer in the pyloric region or prepyloric region, and we must decide, if we can, whether it is benign or malignant. In any case with the x-ray findings of prepyloric ulcer we have come to believe in this hospital that the lesion should be resected since so many prove to be malignant.

To go over the story a little — he was forty years old. That does not help much. The lesion could be cancer at that age. He was a truck driver. That is a nerve-racking occupation. We see many truck drivers with ulcer. The thirteen-year history points toward ulcer. We associate anorexia more frequently with carcinoma than with ulcer,

but if the patient has an ulcer which is causing obstruction, he naturally loses his appetite. Vomiting may go with obstructing ulcer or carcinoma. The negative x-ray films thirteen years previously do not help us. The possibility is raised that he had gastritis at that time. Gastritis can simulate ulcer in almost every respect and give negative x-ray films. His second attack was four years before entry, when he vomited coffee-grounds material. Vomiting such material may be a symptom of either cancer or ulcer. At the present admission he had pain three to four hours after meals which was relieved by soda and milk. That is characteristic of ulcer, but if there is a small area of cancer in a peptic ulcer one may still get the characteristic ulcer pain and get relief from food. Loss of 30 or 40 pounds in weight may occur in obstructing duodenal ulcer. When the patient does not eat well it will lead to loss of weight but cancer must be seriously considered. The red-cell count and hemoglobin are essentially normal which is against advanced cancer but not against a microscopic cancer. Gastric analysis sometimes helps us, but apparently it was not done in this case. Gastroscoy might have helped us, but occasionally there is so much prepyloric spasm one cannot see a prepyloric ulcer or, if it is seen, one cannot always be sure whether it is benign or malignant. Schindler* points out that in gastroscoy the presence of the circulating blood in the living tissue and the presence of a clean base with sharp margins are indicative of benign lesions. Other lesions of the stomach to be considered are benign polyps and lymphoma. With these symptoms and no x-ray evidence of a filling defect a polyp is most unlikely. Lymphoma with an ulceration in it is conceivable but unlikely.

Listing the things in favor of ulcer we can enumerate pain three or four hours after meals, relief by milk and soda, a thirteen year history, a normal red-cell count and hemoglobin, and x-ray evidence of a very small ulcer with converging rugae close to the pylorus, with no infiltration. In favor of cancer stand anorexia, loss of weight and the x-ray appearance of an ulcer possibly in the prepyloric region, particularly the fact that the crater is described as irregular. None of these things are conclusive of either ulcer or cancer. I should like to hear what Dr. Hampton has to say about the x-ray films.

DR. AUBREY O. HAMPTON. The second examination reads a little different from the first examination. In the first the ulcer was thought to be prepyloric and in the second it was thought to be in the pylorus. I believe the second interpreta-

tion is the more accurate of the two. Certainly we were able to fill the duodenum, and in this picture here is the stomach and here the duodenum. It would be quibbling if we did not say that this ulcer is in the pyloric valve. The base of the duodenum is puckered a little as though the lesion involved a little of the duodenum and the stomach is in spasm proximal to the ulcer which is here. I think if we are ever able to be sure this ulcer is directly in the valve.

DR. BENEDICT. As a matter of fact, I have been leaning all along toward the diagnosis of ulcer. Ulcers in the pylorus are usually duodenal and not malignant, furthermore, there are some prepyloric ulcers that are not malignant. I was recently looking up a case of prepyloric ulcer which was resected and proved to be two benign gastric ulcers, one 4 cm. from the pylorus, and the other 1 cm. That does not alter our opinion that they should all be resected if they are prepyloric. Since this lesion is in the pylorus by x-ray and for the other reasons already stated, I will say it is benign.

DR. TRACY B. MALLORY. Does anyone wish to differ with this opinion?

DR. CHESTER M. JONES. I should like to emphasize the importance of a decision to operate rather than the importance of making a diagnosis. An absolute diagnosis is impossible and of minor importance. The decision to resect a lesion that is potentially malignant is the only point to stress in this particular case.

PREOPERATIVE DIAGNOSIS

Duodenal ulcer

DR. BENEDICT'S DIAGNOSIS

Benign pyloric ulcer with obstruction

ANATOMICAL DIAGNOSIS

Carcinoma of the stomach with invasion of the duodenum

PATHOLOGICAL DISCUSSION

DR. MALLORY. This patient was operated on with a preoperative diagnosis of duodenal ulcer, but with the intention of resecting regardless of the anatomical findings. The ulcer lay in the pylorus but extended from it toward the gastric side for a distance of about 1.5 cm. It was not very large. There was absolutely no induration. In the gross it would have been quite impossible by palpation to have recognized it as being malignant. On microscopic examination we found a large central area of peptic ulceration, but on either side of that and in occasional spots on the floor

*Schindler, *Am. J. Gastroscopy*, 343 pp., Chicago: University of Chicago Press, 1937.

of the ulcer definite carcinoma was found. Almost all of it was limited to the mucosal layer and in only one spot was there the slightest invasion below the muscularis mucosa. On the other hand it is not a pure carcinoma in situ, because in the mucosal layer there is definite infiltration between persistent normal glands for a considerable distance and this infiltration of the mucosal layer extends a few millimeters into the duodenum.

DR JONES: Would you be willing to comment on the frequency with which a carcinoma passes the pyloric valve into the duodenum?

DR MALLORY: For many years all the textbooks of surgery and pathology said that carcinomas al-

most never passed the pyloric valve. A few years ago Dr. Castleman examined a series of cases in this hospital in order to check that point and came to a very different conclusion.

DR BENJAMIN CASTLEMAN: About 25 per cent of all the cancers in the region of the antrum show some extension into the duodenum, the distances varying from 3 mm. to 3 cm.* This will be observed only if special care is taken to select blocks for microscopic examination from the extreme margin of the resected specimen.

DR JONES: This fact would seem to be very important in the event of resection.

*Castleman B. Extension of gastric carcinoma into the duodenum. *Ann Surg* 103:348-352 1936.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

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THE NEW HAMPSHIRE MEDICAL SOCIETY
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SUBSCRIPTION PRICES: \$6.00 per year in advance, postage paid, for the United States; Canada, \$7.00 per year; \$8.50 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Tuesday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 5 Parkway Boston, Massachusetts.

HOSPITALS AND—HOSPITALS

In the Hospital Number (March 11, 1939) of the *Journal of the American Medical Association* there are listed certain hospitals as approved for intern-ship and other hospitals as registered but not so approved. One notes with a considerable degree of uneasiness that still other hospitals, not named, were not registered. What the public would like to know is why hospitals are permitted to exist if they are not suitable even for registration.

It is to be noted in the recently published illuminating article by Runnels* concerning obstetric problems that the author limits himself to five conclusions. The first and last are, respectively, that in the United States there has been in recent years a marked reduction in maternal mortality and that, if obstetric conditions were as good in the whole country as they are in one

quarter of the country there would be an annual saving of 2500 lives. The other conclusions concern the great and rapid increase of hospitalization of obstetric patients, the necessity for competent supervision for hospital obstetrics and the great further decrease in maternal mortality in which such supervised hospitalization would result.

This year in Massachusetts there was prolonged discussion before the legislature of the licensing of hospitals, followed by rejection of the proposed bill. It is true that the State already licenses and supervises all hospitals which care for maternity cases, but the standards for license under the present law represent a dangerously low minimum of equipment and fitness. One of the objections to the proposed plan, not always emphasized publicly, was that certain physicians would not be able to earn a living if they could not run their own little hospitals. Regulation by the State would entail so much in the way of equipment, supplies and personnel that the hospital would have to be closed, and thus the physician would lose the chief source of his income. Another objection was that the licensing of hospitals would be just another (useless) restriction on how a doctor should practice medicine. But it is known that abuses have caused a rising tide of feeling to the effect that there should be some control, external to the proprietors, over these institutions, which have become quasi public in character.

It may be that licensing by the State as proposed by the bill is not the best procedure, but it is intolerable that an incompetent or unscrupulous physician should have an extension of the field of his activity, such as the owning of an institution gives, without more control than is exercised now.

At the hearings on the bill some isolated cases of abuse were cited but what is needed before control can be exercised wisely and adequately is a more detailed knowledge of the situation as it exists in Massachusetts today. It is the hospitals not registered by the American Medical Association which are the cause for the greatest concern. Perhaps such a state-wide study might be carried on under the auspices of the Massachusetts Medical Society or the Massachusetts Hospital As-

sociation or by the Massachusetts Department of Public Health. In any case the magnitude and character of the problem should be determined accurately before a specific remedy is advocated. The situation is probably much more serious than anyone now realizes.

HOOTON AND THE FALL OF MAN

EARNEST A. HOOTON, professor of anthropology, Harvard University, amusingly startles the public in an article in *The Atlantic Monthly** concerning man's degenerating evolutionary trends, and takes particularly to task one portion of mankind—the members of the medical profession. Some of his remarks deserve to be repeated and discussed. He says in part:

Medicine has alleviated suffering and prolonged life, but it has, in so doing, also prolonged suffering and nullified the purging effect of natural selection. It has saved hundreds of thousands of debilitated organisms which are adding to the burden of society by reproducing more and worse offspring.

I am not aware that they [medical men] have taken any united professional stand in favor of birth control, nor in the matter of sterilization of the feeble-minded, the insane, and the criminalistic, nor even in the establishment and enforcement of rigorous medical examinations for persons intending marriage. While they have accumulated vast files of medical histories, they have not, for the most part, learned the elementary methods and principles of accurate scientific recording and are usually incapable of analyzing massed data from which valid general conclusions may be drawn. Although the social sciences and all other biological sciences have long relied upon mathematical statistics as the only dependable means of elucidating quantitative or qualitative data affected by a multiplicity of causes, medical science stands aloof in obdurate and self-satisfied ignorance.

These blows at medicine, strong as they sound, are administered in friendly fashion, for Professor Hooton goes on to give medical science "credit for remarkable achievement in the conquest of disease." One wonders how serious he is when he makes such mischievous remarks as the following: "Medicine today is an extension of the maternal instinct mixed up with scientific techniques. It operates in an odor of sanctity and formaldehyde."

It would require a generous amount of space

to comment in full on the conclusions of this article or those incorporated in Professor Hooton's recent work, *Twilight of Man* (New York: G. P. Putnam & Sons, 1939). Many of the conclusions concerning disease are of doubtful validity. Some of the indictments of the medical profession are unquestionably well deserved, many of them demand criticism, and all of them require careful thought. At least it is startling to think that the medical profession may be shouldered with the responsibility not only of the care of the sick and the prevention of illness but also with the care of society and its ills and with the care of the proper evolution of man!

One reads into his work that Professor Hooton believes that the human race is degenerating. Recent trends of world affairs, indeed, have led man to believe so. Perhaps students of history will not agree that the present state of affairs in the world is abnormal. At any rate it appears that we need more convincing proof that mankind is degenerating or even that protection of the weak has interfered seriously with natural selection. One fact is obvious: mankind has survived. To survive in the face of enormous environmental forces means the presence of strong protective mechanisms in the body. It is hard to believe that man is the weakling that Professor Hooton would have us think.

His suggestion that modern methods of handling large masses of data by machinery should be used more and more by hospitals and medical research institutions deserves comment. Are not these methods merely modern, time-saving devices for recording, classifying and describing? Are they an important part of experimental medicine as it was introduced by Claude Bernard? Would their use ever lead to important medical discoveries such as have occurred for several centuries? William Harvey would never have discovered the circulation of the blood if all he had done was to punch-card the data of Galen. The machine has not been built which can substitute for the human reasoning used in performing a useful physiological experiment. When it is built, then perhaps man can allow his brain to atrophy.

Hooton, Earnest A. *The Wages of Biological Sin*. *The Atlantic Monthly* 164: 435-445, 1939.

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PUERPERAL SEPSIS AT TERM

Mrs. F. B., a twenty-one year-old para I at term, was admitted to the hospital June 15, 1912, in active labor of two and a half hours duration.

The patient's past and family histories were not recorded. The last menstrual period began on September 16, 1911, making her due for delivery June 23. The prenatal course had been entirely normal.

The physical examination was normal. The heart was not enlarged, there were no murmurs. The lungs were clear and resonant; there were no rales. The pelvic measurements were normal. The baby was presenting by the breech in the SLA position. The fetal heart was heard best in the left lower quadrant and its rate was 160.

A simple breech delivery was performed under ether anesthesia when the patient was fully dilated after four hours of labor. There were no lacerations. The baby weighed 6 pounds, 8 ounces, and was in good condition. The placenta was delivered intact, the uterus contracted well and there was only a normal loss of blood.

The patient had a smooth convalescence until the fourth night after delivery when the temperature rose to 102°F., the pulse to 115 and the respirations to 25. There was moderate tenderness over the fundus of the uterus. The lochia was very foul. The following night the temperature rose to 105°F., and the pulse to 130. A curettage was performed with a dull curet. A large amount of retained secundines was removed. An intra-uterine douche of sterile water was administered followed by one of alcohol. A uterine culture taken at the time of curettage subsequently revealed colon bacilli and streptococci (type not determined). The patient ran a spiking temperature for the next ten days. She received daily intra-uterine douches of sterile water followed by alcohol.

On July 5, twenty days after delivery a vaginal examination was made. The uterus was of normal size, anterior and freely movable. To the left of the uterus was an indurated, non-tender mass the size of a lime. The right vault was free. During the ten-day interval following this examination the temperature varied from 99 to 100.2°F.

A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

and the pelvic mass increased in size to that of an orange. The patient received hot douches daily. She was discharged home against advice on July 17, 1912. Discharge examination revealed a persistent mass, the size of an apple.

Comment. This case is recorded to illustrate the popular treatment of puerperal infection in 1912. Today cultures would have been taken from the uterus at the onset of the fever, blood cultures would have been taken and the uterus would have been left entirely alone. Curettage in the absence of hemorrhage is entirely outmoded. It undoubtedly did no good in this case and may well have spread the infection. Daily intra-uterine douches of sterile water followed by alcohol was a common routine at that time. These undoubtedly did no good and are never given nowadays. They were not infrequently followed by chills. When one appreciates that whenever an infection of the uterus exists the infected areas are chiefly within the uterine musculature, one realizes that no matter how much alcohol is used it cannot come in contact with these areas as none of it is retained in the uterine cavity. The induration to the left of the uterus when the patient was discharged was evidence of infection of the left parametrium. Such indurated masses almost never demand surgery unless a pelvic abscess develops, which fortunately is not common. When such cases are treated conservatively, the pelvis usually remains free from infection and sterility rarely ever results.

MEDICAL POSTGRADUATE
EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning November 27.

BARNSTABLE

Sunday, December 3 at 4:00 p.m., at the Cape Cod Hospital Hyannis. Complications in Obstetrics Illustrated by Case Histories. Instructor: Christopher J. Duncan. Donald E. Higgins, *Chairman*.

BRISTOL NORTH*

BRISTOL SOUTH (New Bedford Section)

Friday, December 1 at 4:00 p.m., at St. Luke's Hospital, New Bedford. Syphilis in Pregnancy and the Offspring. Instructor: C. Guy Lane. Robert H. Goodwin, *Chairman*.

ESSEX NORTH

Friday, December 1 at 4:30 p.m., at the Lawrence General Hospital, Lawrence. Head and Spine Injuries. Instructor: Walter R. Wegner. John Parr, *Chairman*.

*The course will be omitted November 30 local at the time of the D.

ESSEX SOUTH

Tuesday, November 28, at 4 00 p.m., in the Conference Room of the Salem Hospital, Salem. Indications for Cesarean Section. Instructor Robert L. DeNormandie. J. Robert Shaughnessy, *Chairman*

MIDDLESEX EAST

Tuesday, November 28, at 4 00 p.m., at the Melrose Hospital, Melrose. Head and Spine Injuries. Instructor Donald Munro. Walter H. Flanders, *Chairman*

MIDDLESEX NORTH

Friday, December 1, at 4 45 p.m., at St. John's Hospital, Lowell. The Use of Drugs in the Treatment of Childhood Infections. Instructor Warren R. Sisson. William S. Lawler, *Chairman*

WORCESTER (Milford Section)

Tuesday, November 28, at 8 30 p.m., in the Nurses' Home of the Milford Hospital, Milford. Common Laboratory Procedures in Pediatrics and Their Interpretation. Instructor LeRoy D. Fothergill. Joseph Ashkins, *Chairman*

WORCESTER (Worcester Section)

Friday, December 1, at 8 00 p.m., in the Staff Room of the Worcester City Hospital, Worcester. Complications in Obstetrics, Illustrated by Case Histories. Instructor Judson A. Smith. George C. Tully, *Chairman*

WORCESTER NORTH

Friday, December 1, at 4 30 p.m., in the Nurses' Home of the Burbank Hospital, Fitchburg. Surgical Complications in Obstetrics. Instructor Raymond S. Titus. George P. Keaveny, *Chairman*

DEATHS

HARRINGTON—MICHAEL W. HARRINGTON, M.D., of Springfield, died November 13. He was in his sixty-seventh year.

Born in Ireland, he came to this country sixty years ago. He studied at Holy Cross College and received his degree at Baltimore Medical College in 1901.

He was a fellow of the Massachusetts Medical Society and the American Medical Association.

MOLINE—CHARLES MOLINE, M.D., of Sunderland, died November 15. He was in his sixty-fourth year.

Born in Motala, Sweden, he came to Sunderland when he was twelve years old. In 1896 he graduated from Wiliston Seminary. He attended Harvard University and received his degree from the Harvard Medical School in 1903.

He was a fellow of the American Medical Association and the Massachusetts Medical Society, being secretary of the Franklin County District for twenty years.

His widow and two daughters survive him.

OAK—CHARLES A. OAK, M.D., of Lynn, died November 15. He was in his sixty-first year. He was born and received his early education in Boston, and graduated from Harvard Medical School in 1906.

For twenty-five years he was a member of the surgical staff of the Lynn Hospital and had practiced there for

thirty years. He was a fellow of the Massachusetts Medical Society and the American Medical Association and member of the Radiological Society of North America.

His widow, two daughters and a sister survive him.

ROBERTS—SUMNER M. ROBERTS, M.D., of Boston, was fatally injured in an automobile accident on November 19. He was in his forty-second year.

Born in Dedham, he prepared for college at the Country Day School in Newton. He attended Harvard University and received his degree from the Harvard Medical School in 1925. He was an assistant in orthopedic surgery at the Harvard Medical School, a member of the orthopedic staff of the Massachusetts General Hospital, chief surgeon at the Robert Breck Brigham Hospital and member of the staff of the Faulkner Hospital and of Children's Island in Marblehead.

Dr. Roberts was a fellow of the Massachusetts Medical Society and the American Medical Association. He was president of the Boston Orthopedic Club and held memberships in the American College of Surgeons, the American Academy of Orthopaedic Surgeons and the American Orthopaedic Association.

His widow, a daughter, two sons, his mother, a brother and a sister survive him.

MISCELLANY

VERMONT NEWS

The following new members have been added to the faculty of the University of Vermont College of Medicine. Dr. B. J. A. Bombard, Burlington, associate professor of clinical surgery, Dr. A. F. G. Edgelow, Springfield, Massachusetts, assistant professor of clinical obstetrics, Dr. A. S. C. Hill, Winooski, assistant professor of clinical medicine, Dr. Arthur R. Hogan, Burlington, assistant professor of clinical surgery, Dr. Peter P. Lawlor, Burlington, assistant professor of otolaryngology and rhinology, and clinical instructor in ophthalmology, Dr. Wilhelm Raab, Burlington, assistant professor of clinical medicine, Dr. P. M. Ashton, Springfield, Massachusetts, instructor in clinical obstetrics, Dr. A. P. Barney, Springfield, Massachusetts, instructor in clinical obstetrics, Dr. Nathan R. Caldwell, Burlington, instructor in clinical radiology, Dr. A. J. Crandall, Essex Junction, instructor in clinical surgery, Dr. H. M. Farmer, Burlington, instructor in clinical medicine, Dr. Alfred M. Glickman, Springfield, Massachusetts, instructor in clinical obstetrics, Dr. Theodore H. Harwood, Burlington, instructor in medicine, Dr. Fred S. Kent, Burlington, instructor in clinical medicine, Dr. Robert E. L. Loring, Springfield, Massachusetts, instructor in clinical obstetrics, Dr. Katherine E. McSweeney, Burlington, instructor in clinical medicine, Dr. Watson F. Rogers, Underhill, instructor in clinical medicine, Dr. Stanley S. Stusick, Springfield, Massachusetts, instructor in clinical obstetrics, Dr. Christopher M. Terrien, Burlington, instructor in clinical medicine, Dr. J. G. Thabault, Winooski, instructor in clinical medicine, Dr. L. G. Thabault, Winooski, instructor in surgery, Dr. Frederick C. Thorne, Brandon, instructor in psychiatry, Dr. George C. Tully, Worcester, Massachusetts, instructor in clinical urology, Dr. Fletcher H. White, Burlington, instructor in clinical obstetrics, Dr. Clarence E. Bombard, Burlington, assistant in surgery, Dr. Robert S. Jenks, Burlington, assistant in anatomy, and Dr. John H. McCrea, Burlington, assistant in medicine.

PHRENIC NERVE INTERRUPTION

Phrenic nerve interruption in the treatment of tuberculosis has lately lost much of its former popularity. By it is condemned as being practically useless if not actually harmful. A more discriminating judgment of the operation is urged by J. W. Cutler (Phrenic Nerve Interruption. *Ann. Rev. Tuberc.* 40: 26-54 1939) who has analyzed 122 consecutive phrenic nerve interruptions in his late patients. An abstract of this paper follows:

Claims concerning the value of phrenic nerve interruption are contradictory and confusing. One author reviewed 78 reports involving a total of 7435 operations formed as an independent procedure and found "cures" noted in 23 per cent. On the other hand, Corvillo, using his own experiences and those of several workers also, concluded that the operation is "not efficient, not without danger and causes a loss of precious time."

This wide divergence of opinion is in good part explained by the type of patient treated—phenomenally good results are in relatively early cases and they would undoubtedly have been obtained from bed-rest alone, while in far-advanced cases and in the presence of large, thick-walled cavities success can rarely be expected.

In a consecutive series of 122 tuberculous patients on whom phrenic nerve interruption was performed it was effective on 106 as an independent collapse measure. Many types and varieties of tuberculosis are represented. Sexes about equally distributed. The operation was done 60 times on the left side and 62 on the right. In 65 the interruption was temporary, in 57 permanent.

Evaluation of the operation should be based primarily on the changes that follow in the lung under consideration, as determined primarily by comparative x-ray findings, and not necessarily by the ultimate fate of the patient. The time element, following operation is of extreme importance. The good results of phrenic nerve interruption become evident within the first six months. Good results are more difficult to define; therefore, a three-year postoperative interval as a basis for late results, is not unreasonable.

In the evaluation of phrenic nerve interruption is divided under four main headings: the value of the operation as an independent collapse measure, the value as an adjunct to other collapse measures, complications of the operation and temporary as contrasted with permanent phrenic nerve interruption and their corresponding indications and contraindications.

In retrospect, the cases are classified as "apparently suitable" and "unsuitable." Unsuitable cases include apical cavities 3 or more cm in diameter for the operation is less in the attempt to close apical cavities in which the x-ray has become more or less excavated and adherent to the thoracic wall, dense fibrotic lesions with embedded thoracic wall, dense fibrotic lesions with embedded thoracic wall, dense fibrotic lesions with embedded thoracic wall, dense fibrotic lesions with embedded thoracic wall.

In the present series there were 30 patients with lesions deemed unsuitable for the operation. The contraindications, in the sense that no benefit will follow, can, however, be considered absolute, for occasionally a distinctly good result followed.

Twenty-one patients fell into the "apparently suitable" category and were evaluated as follows:

Improved (52 per cent) No material x-ray evidence of improvement in the tuberculous lesions was noted within three to six months after the operation or an actual increase in the disease. Lack of improvement was observed in all kinds of cases with "apparently suitable" lesions, including both cases of early limited infiltrations

without x-ray evidence of cavity and cases of advanced disease.

Improved (34 per cent) Cavity was either closed or reduced in size or there was x-ray evidence of significant clearing with lessening of toxemia and improvement in well-being. However, in only 14 of the 24 cases in this group did the improvement result in the stabilization of the lesion so that no further therapy was required. In the remaining 10 improvement, marked at first, was in time followed by serious relapse.

Cleared (14 per cent) Clearing of the disease in the lung except for some fibrous strands and a few small sharply defined moderately dense spots. There were cavities of varying sizes in 8 and infiltration without x-ray evidence of cavity in 2. The result followed so shortly after operation and in such manner as to leave little doubt that the paralysis of the diaphragm was the responsible factor. The lungs have remained clear over an average period of more than 6 years after operation.

No concrete conclusions could be reached as to the type of case among the "apparently suitable" patients in which the operation can be undertaken with reasonable assurance of success. Good results were obtained in advanced disease and in unexpected situations. On the other hand failures were encountered in minimal cases. In general good results were observed more frequently when the major lesion was situated below the clavicle, and when the cavity was isolated, thin-walled and surrounded by nearly normal lung tissue.

The relative value of phrenic nerve interruption as an alternative to artificial pneumothorax and thoracoplasty is considered. In the majority of cases in which phrenic nerve interruption was used as an alternative to pneumothorax the operation was either a useless undertaking or relapse followed an initial improvement. In those cases in which bilateral pneumothorax ultimately became necessary selective collapse could be established in only 12 out of 28 patients. Time wasted on phrenic nerve interruption was largely responsible for the formation of extensive adhesions. Phrenic nerve surgery should not be looked on as a substitute for pneumothorax, but must be regarded as a supplementary form of therapy.

More serious is the question of phrenic nerve interruption in preference to thoracoplasty. Of 31 patients in this series suitable for an immediate thoracoplasty but subjected to phrenic nerve interruption in the hope of avoiding thoracoplasty 3 died from hemoptysis and 3 from progressive tuberculosis and 7 more became hopeless invalids. In retrospect, these tragedies might have been avoided had thoracoplasty been performed promptly when conditions were most favorable. The important thing is not to resort to a phrenic nerve operation when thoracoplasty is plainly indicated and not to delay thoracoplasty beyond the time when the phrenic nerve operation has accomplished its maximum good.

Phrenic nerve interruption was carried out also in 16 patients either as an adjunct to other collapse measures or in the treatment of certain complications of pneumothorax therapy including ineffective pneumothorax, hemoptysis, troublesome cough, discontinued pneumothorax therapy, spontaneous pneumothorax, empyema, cavities. The operation accomplished the desired result in about one third of these patients.

Complications of phrenic nerve interruption must be taken into consideration. In the present series significant complications attributable to the operation were encountered in 6 with death in 2. Cardiac failure, which accounted for the 2 deaths, was the outstanding compli-

cation Other important complications were interference with the cough mechanism (2 patients) and gastric disturbances (belching and a sense of fullness in the stomach), annoying but not serious (3 patients) The fact remains, however, that the treatment of tuberculosis does not always permit a safe and sure choice of therapy Phrenic nerve interruption may, in individual cases, prove to be accompanied by the least risk

Both temporary and permanent phrenic nerve interruption have their place A temporary phrenic nerve interruption is indicated when the problem is of an emergency nature, as in hemorrhage or active disease requiring immediate collapse therapy when other collapse measures cannot be instituted at the moment, and when other collapse measures, such as pneumothorax or thoracoplasty, are in prospect A permanent phrenic nerve operation is indicated when the operation is carried out as the sole therapeutic measure in the attempt to cure the patient after other collapse procedures have been considered unsuitable, or are plainly contraindicated

The danger today is not that too many phrenic nerve operations will be performed or that they will be undertaken in an indiscriminate manner, but that the operation will be discarded This would be unfortunate, for phrenic nerve interruption appears to have value in 15 to 25 per cent of patients At times it may be the simplest means for saving a patient's life The operation, however, should be restricted to properly selected cases — Reprinted from *Tuberculosis Abstracts*, November, 1939

MASSACHUSETTS PSYCHIATRIC SOCIETY

The annual meeting and dinner of the Massachusetts Psychiatric Society was held on Thursday, November 2, at 6:30 p.m. at the University Club, Boston Dr Karl Bowman, formerly associated with the Boston Psychopathic Hospital and now director of the Psychiatric Division, Bellevue Hospital, New York City, spoke about the Desmond Bill, a law recently passed in New York relative to the psychiatric examination of prisoners

The officers elected for 1939-1940 are as follows: president, Dr William A Bryan, vice president, Dr Harlan L Paine, secretary-treasurer, Dr W Franklin Wood, councilors, Drs Harry C Solomon and Clifton T Perkins

NOTICES

BOSTON DISPENSARY

A talk on "The Psychology of the Hard of Hearing" will be given at the Boston Dispensary by Mr John C G Loring on Friday, December 1, at 9 a.m.

CARNEY HOSPITAL

The monthly meeting of the John T Bottomley Society will be held at the Out-Patient Department of Carney Hospital on Tuesday, November 28, at 11 a.m.

PROGRAM

Coramine, a film produced by Audio Productions, Incorporated, with pharmacological scenes prepared by Ciba Research Laboratories, will be shown

WILLIAM J MACDONALD, M.D., *Secretary*

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, November 29, from 2 to 4 p.m. Drs Elliott C Cutler and Soma Weiss will speak on "The Unconscious Patient Syncope."

A clinicopathological conference, conducted by Dr Elliott C Cutler, will take place from 4 to 5 p.m.

Physicians and students are cordially invited to attend

ELLIOTT C CUTLER, M.D., *Secretary*

BOSTON DOCTORS' SYMPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide, former concertmaster with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, etc.

Thursday at 8:30 p.m., in Studio A, Station WME 70 Brookline Avenue, Boston Those interested in becoming members should communicate with Dr Julius Loma Pelham Hall Hotel, Brookline (BEA 2430)

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Ether Dome of the Massachusetts General Hospital, on Tuesday, November 28, at 5:00 p.m.

PROGRAM

Coagulation Factors Dr J D Stewart.
Changes in Blood Pressure and Pulse Rate on Stimulation of the Autonomic Nuclei in the Human Hypothalamus Dr J C White.
Studies of Muscle Function in Rheumatoid Arthritis Drs A O Ludwig, C L Short and R S Schwab

HENRY K BEECHER, M.D., *Secretary*

SUFFOLK DISTRICT MEDICAL SOCIETY

There will be a meeting of the Suffolk District Medical Society at the Boston Medical Library, 8 Fenway, on Wednesday evening, November 29, at 8:15

PROGRAM

The Theory and Practice of Massive Dose Chemotherapy by the Intravenous Drip Method in the Treatment of Early Syphilis Drs William Leifer, Louis Chargin and Harold T Hyman

MILTON H CLIFFORD, M.D., *Secretary*

MASSACHUSETTS DEPARTMENT OF CIVIL SERVICE AND REGISTRATION

MEDICAL ADVISER, DEPARTMENT OF INDUSTRIAL ACCIDENTS

Director of State Civil Service, Ulysses J Lupien, has recently announced that a competitive examination will be held on January 6 to find eligibles for appointment to the position of Medical Adviser, Department of Industrial Accidents The minimum salary is \$4200 a year, the maximum, \$5100 The duties are as follows: to examine medical testimony given by physicians and technicians at formal proceedings, to make physical examinations of injured workmen and submit opinions and diagnoses as to disability and causal relation to injury, to advise the Industrial Accident Board as to the selection of competent industrial-disease referees and impartial physicians, to interpret medical problems and terminology for the members of the Board, to systemize and supervise the personnel of the medical unit of the department The appointees will be permitted to carry on private practice to such extent as may be permitted by the Board.

is approved by the Department of Industrial Ac

entrance requirements are as follows: applicants: physicians licensed to practice medicine by the state Board of Registration in Medicine and must have been members of the medical or surgical hospital approved by the American College of

objects and weights are as follows: training and ce, 2 practical questions 3 total 5 Applicants must obtain at least 70 per cent in each subject of the exam in order to become eligible. Physical fitness determined by physical examination. Last date for filing applications is Saturday December 23 at noon.

ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

regular clinical conference and meeting of the staff of England Hospital for Women and Children held at the hospital on Thursday, December 7 at

Dr P. Cahill will be the chairman in charge of the and Dr Edgar C. Yerbury director of mental will be the guest speaker

LAURA H. MUIR, M.D., *Chairman*

K DISTRICT MEDICAL SOCIETY

at meeting of the Norfolk District Medical Society held in the Hotel Somerset, Boston Tuesday December 28 at 8:15 p.m.

PROGRAM

possession of the Work of Certain Committees of the Massachusetts Medical Society: Committee on Ethics and Discipline. Dr Robert L. DeNormandie. Committee on Public Relations. Dr Michael A. Tighe. Committee on State and National Legislation. Dr Charles C. Lund.

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FRANK S. CRUICKSHANK, M.D., *Secretary*

HOSPITAL CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER PROVISIONS OF THE SOCIAL WELFARE ACT

DATE	ORTHOPEDIC CONSULTANT
December 1	Albert H. Brewster
December 4	Harold C. Bean
December 6	William T. Green
December 12	Mark H. Rogers
December 14	George W. Van Gorder
December 15	John W. O'Meara
December 18	Francis A. Slowick
December 20	Garry deN. Hough, Jr
December 21	Eugene A. McCarthy
December 22	Paul L. Norton

WILMINGTON STATE HOSPITAL

pathological staff conference will be held at the State Hospital, Waltham on Wednesday December 29 at 8:00 p.m.

PROGRAM

A Case Presenting Special Psychiatric and Neurological Features from Both the Clinical and Pathological Aspects. Dr Clementine McKeon and Dr Richard C. Wadsworth. Discussed by Dr Ira T. Nathanson and Dr Paul I. Yakovlev

All interested physicians are cordially invited to attend.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY NOVEMBER 27

MONDAY NOVEMBER 27

12:15 p.m.-1:15 p.m. Clinicopathological conference. Dr S. Bert V. Bosch. Peter Bent Brigham Hospital amphitheater.
3:15 p.m. New England Heart Association. Massachusetts General Hospital

TUESDAY NOVEMBER 28

9-10 a.m. X-ray Demonstration. Dr Alice Estlin. Pratt Diagnostic Hospital.
10 a.m.-12:30 p.m. Boston Dispensary tumor clinic.
11 a.m. Carney Hospital. John T. Bottomley Society.
12:15 p.m.-1:15 p.m. X-ray conference. Dr Merrill C. Soman. Peter Bent Brigham Hospital amphitheater.
5 p.m. Massachusetts General Hospital. Hospital Research Council.
8:15 p.m. Norfolk District Medical Society. Hotel Somerset, Boston.
8:15 p.m. Visualization of Placenta in Utero. Dr A. Louis Dippel. Boston Lying-in Hospital.

WEDNESDAY NOVEMBER 29

9-10 a.m. Hospital case presentation. Dr S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.
12 m. Clinicopathological conference. Children's Hospital amphitheater.
2 p.m.-4 p.m. Joint medical and surgical clinic. Peter Bent Brigham Hospital.
8:15 p.m. Suffolk District Medical Society. Boston Medical Library. 8 Fenway Boston

THURSDAY DECEMBER 1

9 a.m. "The Psychology of the Hand of Hearing." John C. O. Loring. Boston Dispensary.
10 a.m.-12:30 p.m. Boston Dispensary tumor clinic.
12 m. Civil and medical of the Children's Medical Service, Massachusetts General Hospital. Ether Dome.
12 m. Urological conference at the Massachusetts General Hospital, lower amphitheater. Out-Patient Department.

FRIDAY DECEMBER 2

10 a.m.-12 m. Medical staff rounds of the Peter Bent Brigham Hospital. Conducted by Dr. Soma Weiss

*Open to the medical profession.

NOVEMBER 24.—Boston Dispensary. Luncheon meeting of the clinical staff. Page 753, issue of November 9.

NOVEMBER 25.—Joseph H. Pratt Diagnostic Hospital. Page 58, issue of November 9.

NOVEMBER 27.—New England Heart Association. Page 798, issue of November 16.

NOVEMBER 28.—Boston Lying-in Hospital. Page 797, issue of November 16.

NOVEMBER 28.—Massachusetts General Hospital. Hospital Research Council. Page 840.

NOVEMBER 28.—Carney Hospital. John T. Bottomley Society. Page 840.

NOVEMBER 28.—Peter Bent Brigham Hospital. Joint medical and surgical clinic. Page 840.

NOVEMBER 29.—Metropolitan State Hospital. Notice above.

DECEMBER 1.—Boston Dispensary. "The Psychology of the Hand of Hearing." John C. O. Loring. Page 840.

DECEMBER 2.—American Board of Obstetrics and Gynecology. Page 1019, issue of June 15.

DECEMBER 3.—Massachusetts Hospital Association. Page 798, issue of November 16.

DECEMBER 6.—Wachusett Medical Improvement Society. Page 795, issue of November 16.

DECEMBER 6.—New England Obstetrical and Gynecological Society. Page 799, issue of November 9.

DECEMBER 7.—New England Hospital for Women and Children. Notice above.

DECEMBER 8.—William Harvey Society. Page 677, issue of October 9.

DECEMBER 14.—Fletcher Association of Physicians. 8:30 p.m., Hotel Bartlett, 115 Central

JANUARY 6 JUNE 8-11 1940 — American Board of Obstetrics and Gynecology Page 169 issue of July 27 and page 795 issue of November 16
 JANUARY 22-25 1940 — American Academy of Orthopedic Surgeons Hotel Statler Boston
 FEBRUARY 11-14 — International College of Surgeons Page 759 issue of November 9
 MARCH 2, JUNE 8 and 10 — American Board of Ophthalmology Page 719 issue of November 2
 MARCH 7-9 1940 — The New England Hospital Association Hotel Statler Boston
 MAY 14 1940 — Pharmacopoeial Convention Page 894 issue of May 25
 JUNE 7-9 1940 — American Board of Obstetrics and Gynecology Page 1019 issue of June 15

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 3 1940 — Semi annual meeting Combined meeting with Essex South. Danvers State Hospital Hathorne 7 p.m.

ESSEX SOUTH

DECEMBER 6 — Pyelonephritis and Its Relation to Other Inflammatory Diseases of the Kidney Dr. Soma Weiss. Salem Hospital Salem

JANUARY 3 1940 — Head Injuries Dr. John S. Hodgson Danvers State Hospital Hathorne

FEBRUARY 14 — Cough Sputum Hemoptysis — How shall we be investigated? Dr. Reece H. Berts Essex Sanatorium Middleton

MARCH 6 — Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections Dr. Champ Lyons Lynn Hospital Lynn

APRIL 3 — Addison Gilbert Hospital Gloucester

MAY 8 — Annual meeting Salem Country Club Peabody

HAMPSHIRE

JANUARY 10 1940

MARCH 13

MAY 8

All meetings are held at 11 30 a.m. at the Cooley Dickinson Hospital Northampton

MIDDLESEX EAST

JANUARY 10 1940

MARCH 20

MAY 15

Meetings are held at 12 15 p.m. at the Unicorn Country Club Stonham

NORFOLK

NOVEMBER 28 — Page 841

PLYMOUTH

JANUARY 18 1940 — Brockton Hospital Brockton

MARCH 21 — Goddard Hospital Brockton

APRIL 18 — State Farm

MAY 16 — Lakeville Sanatorium Lakeville

SUFFOLK

NOVEMBER 29 — Scientific meeting Treatment of Syphilis Dr. Harold T. Hyman Dr. Louis Chargin and Dr. William Leifer of New York City Page 840

JANUARY 31 1940 — Scientific meeting Subject to be announced later

MARCH 27 — Scientific meeting Symposium on Ulcerative Colitis and Diarrhea Under the direction of Dr. Chester M. Jones

APRIL 24 — Annual meeting in conjunction with the Boston Medical Library Election of officers. Program and speakers to be announced later

BOOKS RECEIVED FOR REVIEW

Principles of Development A text in experimental embryology Paul Weiss 601 pp New York Henry Holt & Co., 1939 \$5.00

Health for New York City's Millions An account of activities of the Department of Health of the City of New York for 1938 with comparative vital statistics tables Edited by Savel Zimand. 295 pp New York Department of Health, 1939

Blood Groups and Blood Transfusion Alexander S. Wiener Second edition 306 pp Springfield, Illinois, and Baltimore Charles C. Thomas, 1939 \$5.00

Psychobiology and Psychiatry A textbook of normal and abnormal human behavior Wendell Muncie 739 pp St. Louis C. V. Mosby Co., 1939 \$8.00

Textbook of Nervous Diseases Robert B. L. L. lated and enlarged by Webb Haymaker German edition 838 pp St. Louis C. V. 1939 \$10.00

Medical Record Visiting List of Physicians 1940 Revised. Baltimore William Wood & \$2.00

Ophthalmology Cho Medica 20 Burton C. pp New York Paul B. Hoeber, Inc., 1939

Tumors of the Skin Benign and malignant Eller 607 pp Philadelphia Lea & Febiger, 1939

The Vitamins A symposium, arranged under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association 637 pp Chicago American Medical Association \$1.50

Sixty first Annual Report of the Department of Health of the State of New Jersey, 1938 406 pp Department of Health, New Jersey

Fractures Paul B. Magnuson Third edition. Philadelphia, Montreal, London J. B. Lippincott 1939 \$5.00

A Handbook on Diabetes Mellitus and its Treatment J. P. Bose. Third edition 272 pp. C. Thacker, Spink & Co., Ltd., 1939 Rs. 7-8

Psychopathia Sexualis A medico-forensic study and von Krafft-Ebing Twelfth edition 626 pp. New York Pioneer Publications, Inc., 1939 \$3.00

BOOK REVIEWS

Nitrous Oxide-Oxygen Anesthesia McKesson-Clement viewpoint and technique F. W. Clement. 2 Philadelphia Lea & Febiger, 1939 \$4.00

This book "is dedicated as a memorial to the life and achievements of Dr. E. I. McKesson" and sets his philosophy and the technic of methods for the nitrous oxide and oxygen which he worked out during his lifetime. It is an authoritative treatise on this method of anesthesia, but its value as a practical guide for the physician is somewhat lessened by the fact that in the detailed description of technic the use of the McKesson method is only described.

A complete explanation and rationalization of the use of anesthesia is given. Respiration and muscular activity are stressed while phonation and color are shown to be deceptive and unreliable as they bear no relation to the depth of anesthesia in different individuals. Preanesthesia, charting and signs of the onset of shock are well presented.

An explanation of the role of carbon dioxide in respiration is treated in a most thorough manner. It is shown that there is no "fixed relationship between cyanosis and physiological anoxemia, a fact of great importance in the clinical interpretation of cyanosis." The famous "secondary saturation" is carefully described, explained and declared to be less dangerous than essential oxygen want during prolonged deep narcosis.

Dr. Clement reiterates the importance of a clear way in many of his discussions, especially those concerning special operations. He shows clearly that obstruction to breathing causes alterations of the normal physiological processes. His methods of treating such obstructions are rational and simple, and show great clinical knowledge. Although the author gives elaborate instruction for administering nitrous oxide and oxygen for major abdominal operations, he admits that even the McKesson method, in his hands, will not produce the relaxation obtained with a good ether or spinal anesthesia.

there is no doubt left in the reader's mind regarding initial ability or knowledge of the author in dealing with nitrous oxide and oxygen anesthesia. His presentation of the subject is most convincing and the book is a tribute to the late Dr. McKesson and should be required reading for anesthetists. The knowledge which he so painstakingly acquired it should be read and preferably by every anesthetist who at any time uses this form of anesthesia.

Head and Head Pains. A ready reference manual for physicians. Walton F. Dutton, 301 pp. Philadelphia: F. A. Davis Co., 1939. \$4.50.

The primary purpose of the author of this book is to bring the medical profession to an appreciation of the importance and significance of headache. He believes that the sources of pain compare in frequency to those symptoms in the large majority of patients who seek medical aid and second that the major concern of the scientific worker is centered in the problems of diagnosis, etiology, pathology and therapeutic technique in dealing with disease with the implication that the cause of the disease must be discovered if cure or amelioration is to be brought about.

The author deplores the custom of self-medication for the relief of symptoms which too often leads to postponement of essential management of a case, with disastrous results. A good description of the anatomy and functions of the several systems of nerves prepares the reader for the adoption of certain defined methods of study in order to solve the etiologic problems in cases with different types of headache.

A greater portion of the book is given to brief descriptions of nearly two hundred and fifty diseases and neural disturbances in which headache appears as a prominent symptom. Consideration is given to remedies used to relieve suffering.

This book is worthy of a place in the physician's library because it is well written and covers the ground. A question may be raised as to whether the emphasis on the relief of a symptom may not divert the attention of those doctors who are not well trained from adequate study of a disease which can only be properly treated on knowledge of its pathology.

Cerebral Vascular Diseases: Diagnosis and treatment. William S. Collens and Nathan D. Wdewsky. 243 pp. Springfield, Illinois, and Baltimore: Charles C. Thomas, 1939. \$4.50.

This monograph handles effectively though by no means exhaustively the diagnosis and treatment of cerebral arteriosclerosis and thromboangitis obliterans. In the pathology of arteriosclerosis, the authors lean toward Winternitz's theory of local fault in the vaso-motor system. The best chapters of the book are those on the signs and symptoms of examination and the treatment of the patient. The authors review all methods of increasing the circulation to the extremities. However, they devote most space to intermittent venous occlusion, the treatment which they have devised. This is done, with detailed case reports illustrating the method. Other types of treatment are not so well handled. The forms of heat are proposed without reference to their deleterious effects, except for burns. More satisfactory offer no help in evaluating such unusual quoted cases as the subcutaneous introduction of oxygen and carbon dioxide or the intra-arterial injection of medicinal

nature. Unusual but important organic lesions such as cervical rib and periaortitis nodosa are given brief and indecisive mention. Functional disorders are better described but could stand more detailed presentation.

The addition of a chapter on the treatment of varicose ulcers by intermittent venous occlusion without any other discussion of the varicose problem hardly seems justified in a text devoted to arterial diseases.

Operative Orthopedics. Willis C. Campbell, 1154 pp. St. Louis: The C. V. Mosby Co., 1939. \$12.50.

The author has had an extensive operative experience and therefore is well equipped to produce a book of this type.

The introductory chapter is confined to a consideration of the physiology and pathology of bones and joints; then follows a chapter on the apparatus used in the Campbell Clinic.

The rest of the book is devoted to a description of various orthopedic conditions and of the different types of operative procedures that are standardized and commonly used. The division of subjects follows rather closely the author's textbook of orthopedic surgery and includes fresh fractures, malunited fractures and non-unions.

The chapter on arthroplasty is very complete, as would be expected because of the author's personal interest in this subject and his extensive writings. It is chiefly a summary of his own work, although he describes the technique of other authors.

The chapter devoted to the correction of deformities due to infantile paralysis is well done and timely since it constitutes an important part of orthopedic surgery. The author describes the various types of standard operations, giving credit to the different authors and using some of their drawings and cuts. At the same time he has emphasized the methods that he commonly uses.

The reproductions of x-ray plates and the drawings are adequate and freely used and they complement the text very well. There is a bibliography at the end of each chapter and a very good index at the end of the book. This is a very good and timely book.

A Textbook of Surgery. By American authors. Edited by Frederick Christopher. Second edition revised. 1695 pp. Philadelphia and London: W. B. Saunders Co., 1939. \$10.00.

Since its first appearance in 1936 this volume has become the favorite textbook of surgery of many American medical students. There are one hundred and eighty-eight contributors, almost all of them associated in a teaching capacity with medical schools. In its pages the whole of surgery including gynecology, urology and orthopedics is covered. Of course no single volume can encompass the entire field of surgery today and it is questionable if the term "textbook" is wholly advisable. Perhaps *An Introduction to Surgery* would be more suitable as such its excellence is unquestioned. Most of the criticism which a careful survey of the volume brings forth concerns omissions rather than errors. Some of those which struck the reviewer as of particular importance follow.

The question of sprains and contusions is dismissed in a few paragraphs. These common injuries might well have received more attention.

In the section on trigeminal neuralgia alcohol injection is summarily dismissed as of little benefit, and operation advised as soon as the diagnosis is established. It should be mentioned that many neurological surgeons believe that alcohol injections should precede operation.

The book fails to live up to its avowed comprehensive

whenever possible so that the patient will have actual experience with anesthesia of the face and be able to weigh the disadvantage of numbness against the advantage of freedom from pain. No mention is made of the ingenious apparatus of Kirschner for the coagulation of the gasserian ganglion. This has not been used in this country but has apparently been very successful in Europe.

In the section on sciatica no mention is made of the operation of Ober division of the fascia lata. Although a relatively new procedure, it has been received with considerable favor and should at least be mentioned as a method of treatment for this otherwise often baffling condition.

In the section on cancer of the breast the procedure of roentgen castration of all patients who are still menstruating is dismissed in a paragraph and is not recommended as a routine. This procedure is now accepted as of great value and is practiced as a routine in most Eastern clinics.

The section on chronic fat necrosis of the female breast is likely to leave the student with the impression that it can be differentiated from carcinoma in most cases. This is far from true, as any surgeon of experience can testify. Reference should be made to the work of Dunphy in this connection and it should be emphasized that the condition is almost invariably indistinguishable, in the gross form, from carcinoma.

The described method for carrying out closed drainage in cases of empyema of the chest will almost inevitably result in pyopneumothorax. It has long been established that the presence of air in an empyema cavity facilitates the absorption of bacterial toxins and should be avoided.

The reviewer was astonished to find in the otherwise adequate discussion of acute appendicitis no mention of referred or 'rebound' tenderness which is generally considered to be one of the most important, if not the most important, single sign of the disease.

In the thirty seventh chapter entitled 'Aseptic Surgical Technique,' the traditional sterilization of linen in sealed steel drums is described and illustrated. The inadequacy and dangers inherent in such methods of sterilization have been well established by the researches of Walter and others. Furthermore, 90 per cent alcohol is advocated as a rinse for the surgeon's hands after scrubbing and for the removal of iodine from the operative field. It has been known for at least fifty years that 95 per cent alcohol is of very little value as an antiseptic, it is far inferior to 70 per cent alcohol, which itself is not particularly good.

These errors, however, are of relatively minor importance and do not detract from the fundamental excellence of the volume as a whole. Undoubtedly they will be corrected in future editions. The popularity of the book is deserved and should continue.

Provoked Alimentary Hyperglycemia. The mechanism of the tolerance test. Joseph M. Flint. 37 pp. *The Effect of the Macallum Loughton Duodenal Extract Upon Hypophyseal Diabetes.* Joseph M. Flint and Louis Michaud. 77 pp. London, Ontario: A. B. Macallum, 1939.

The first of these two articles, which are bound in one volume, is a summary of literature and also, to some extent, of experimental observations dealing with the ordinary glucose tolerance test. Using the angiotomy method, the author concluded that in the ordinary glucose tolerance test there is a shift of function between the liver and intestines at the beginning and at the end of the reaction, such that the liver and intestines exchange roles as yielding and retaining organs in relation to the blood sugar. Thus on the appearance of carbohydrate in the

duodenum, absorption of sugar begins and its concentration in the intestine mounts until it passes the retention point, when glucose is yielded to the portal radicals. Increase in sugar concentration in the portal blood is stimulus that induces the liver to reduce its yield of sugar to the zero point and to begin to return sugar. Then the blood sugar falls below normal, the relation is reversed again. He regards diabetic tolerance tests as exaggerations of the same factors in regulation.

In the second article observations making use of Macallum Loughton extract of the duodenum are reported. This extract is regarded as a stabilizing and synergizing factor to insulin, and an antagonist to the anterior portion of the pituitary gland, tending to anchor blood sugar to normal levels and maintain its stability. When given to diabetic patients by mouth or combined with insulin, it may overcome the insulin resistance of the impaired utilization which are present in hypophyseal diabetes. To the reviewer, it seems that distinctions between hypophyseal and pancreatic diabetes have less significance than formerly, because Young has demonstrated that the production of diabetes by means of injections of crude pituitary extract is brought about by destruction of the islands of Langerhans.

Both articles contain discussions of many of the classic experiments dealing with carbohydrate metabolism, particularly the recent experiments of Young. The actual experimental data reported, however, could be discussed more briefly with advantage to the reader.

Clinical Diagnosis by Laboratory Methods. A working manual of clinical pathology. James C. Todd and Arthur H. Sanford. Ninth edition. 841 pp. Philadelphia and London: W. B. Saunders Co., 1939. \$6.00.

This, the ninth edition of a well known and standard textbook on clinical laboratory methods, has been completely brought up to date. Some obsolete procedures in urinalysis have been deleted, and new tests have been included, such as the complete technic of Bodansky for the determination of phosphate and phosphatase, the complete technic of Power and Wakefield for sulfates, the hippuric acid test for liver function, the technic for the determination of serum lipase, and that for ascorbic acid as sulfanilamide in blood and urine.

There has been a complete revision of the material on serodiagnostic tests for syphilis. Besides this, many minor changes and several illustrations have been added. In regard to illustrations, in the new colored frontispiece the blues are too brilliant and the reds are too pale, as is often the case. This plate does not compare with some of the older plates still retained in the book.

The volume is a most useful one, and is doubtless one of the best we have at present on the subject.

The New International Clinics. Original contributions, clinics, and evaluated reviews of current advances in the medical arts. Edited by George M. Piersol. Vol. 2, N. S. 2. 321 pp. Philadelphia, Montreal and New York: J. B. Lippincott Co., 1939. \$3.00.

This volume covers a wide range of subjects. Vitamin from the neurological and psychiatric aspects are discussed, and there is an article on pellagra. Treatment of anemia, the functions of the pituitary gland and cancer of the male reproductive organs are among the large group of excellent contributions by well known authors.

The New England Journal of Medicine

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VOLUME 221

NOVEMBER 30, 1939

NUMBER 22

MASSACHUSETTS MEDICAL SOCIETY

Section of Obstetrics and Gynecology

MATERNAL MORTALITY STUDY IN MASSACHUSETTS FOR 1938*

RAYMOND S. TITUS, M.D.†

BOSTON

It is likely possible that some of those present unfamiliar with the maternal mortality study may have been carried out by this section in the last two years. Three years ago the Division of Hygiene of the Massachusetts Department of Public Health asked the officers of the section to conduct such an investigation. Permission was granted from the Council, and in 1937 and 1938 records of all the maternal deaths in Massachusetts were investigated by members of this section. This study is to be continued for three more

years. It is likely possible that some of those present unfamiliar with the maternal mortality study may have been carried out by this section in the last two years. Three years ago the Division of Hygiene of the Massachusetts Department of Public Health asked the officers of the section to conduct such an investigation. Permission was granted from the Council, and in 1937 and 1938 records of all the maternal deaths in Massachusetts were investigated by members of this section. This study is to be continued for three more

The mortality rate in Massachusetts for 1938 and that in Boston (3.6) are virtually identical. This indicates that, so far as figures are significant, the practice of obstetrics in rural communities is quite as good as, but no better than, that in the big cities with their large hospitals and medical schools. On the other hand, it must be realized that some city institutions do far better work than is done generally. The Boston Lying-in Hospital, for instance, had a death rate in 1938 of 1.1 per 1000 live births. Obviously, then, the quality of obstetric practice in this hospital is far superior to that in the State at large and in the rest of Boston. It should be our aim to meet this excellent figure.

Obstetric practice in Massachusetts cannot be improved unless we know where the trouble lies. We must consider the separate factors entering into obstetric mortality, namely the patient, the medical profession and the hospital.

As to the patient, our study of the records demonstrates that a certain number of deaths are due solely to the patient's neglecting to consult a physician on the appearance of unusual symptoms. There must be more adequate education of the public, and better standards of prenatal care must be established and maintained. It must never be the case that a woman is unable to obtain intelligent prenatal care for lack of money or for any other reason.

The primary purpose of the investigation is to find out the facts, the hope is to improve the practice of obstetrics in Massachusetts, where it is, unfortunately, far from perfect. Many criticisms have been made, but if we commence with the premise that medicine is practiced solely for the benefit of the patient and that hospitals have no right to exist unless they provide the patients receive the best possible care, then the criticism of the practice of obstetrics in this State is justifiable. Hospitals are not established for the convenience of physicians but for the care of patients, and if the latter in certain hospitals do not receive the best, the hospitals in question are open to condemnation.

The year 1938 showed an improvement over 1937 in the extent of maternal mortality. In 1937 the rate was 4.1 per 1000 living births, in 1938 it was 3.7. It is at least conceivable that the publication of this study has resulted from what the section has had a stimulative effect on the medical profession and on the hospitals and so has

*Section meeting was held and the following three papers read at annual meeting of the Massachusetts Medical Society, Worcester, Mass., June 8, 1939.
†77 Section of Obstetrics and Gynecology

The next share of responsibility devolves upon the medical profession. The study of these cases showed that some lives were lost because of the attending physician's ignorance or neglect. This situation can be remedied only by better obstetric education and by a more conscientious attitude on the part of physicians toward their patients.

The third responsible factor is the hospital. Not all hospitals are equally equipped or equally well staffed, and many hospitals that are both well equipped and well manned are not adequately supervised. Fortunately, the day when the doctor can do as he pleases with the individual patient is passing. He can no longer withstand the criticism of his fellow practitioners when he knows that he is indulging in practices in obstetrics that he would reject in surgery. The staffs of the hospitals must be better supervised. Hospital authorities must realize that their primary responsibility is to give their patients the best possible obstetric care. Adequate consultation in obstetric complications can easily be made available to any hospital desiring it.

This paper does not attempt to analyze in statistical detail the obstetric work carried on in 1938. Briefly, 282 fatal cases were reviewed, compared with 325 in 1937. Six of these were found to be non-obstetric, so that the actual total is 276 maternal deaths, or a mortality rate of 37 per 1000 live births. The rate for 1927 was 63, that for 1936 49 and that for 1937 41. Thus it would appear that the mortality rate is steadily decreasing, but it must be remembered that the number of cases of sepsis in 1938 was quite low, a fact which lessens the significance of the low mortality rate. Furthermore, it should not be forgotten that Rhode Island, as mentioned above, had a mortality rate in 1938 of only 26.

Sepsis still caused the greatest number of puerperal deaths in 1938, namely 66. Most of these followed operative deliveries, showing that less unnecessary operating is needed. The more conservative we become the less sepsis there will be. The records reveal that a physician in one institution delivered operatively over 25 per cent of his patients, clear evidence that in some parts of the State there has been too much operative interference.

There were 5 deaths from pernicious vomiting in 1938, compared with 4 in 1937. Any patient who dies of pernicious vomiting does so either because she does not, through ignorance, present herself for treatment soon enough or because she does not receive adequate care after being hospitalized. Therefore, since the great majority of deaths from this cause are due to delay in giving proper treat-

ment, those here cited must be classed as preventable.

There are still too many deaths from anesthesia there were 9 in 1938.

Ectopic pregnancy will always cause a certain number of deaths. There were 12 last year, in 5 of which the patients were not operated on. In some cases the fault lay with the physician, who did not recognize that irregular bleeding during pregnancy may indicate ectopic pregnancy, in others the patient's ignorance of the same fact was to blame.

There were 13 deaths in 1938 due solely to surgical causes. Too often when a woman is pregnant it is forgotten that she is subject to the same surgical ailments that other women have. The sooner the medical profession realizes that a pregnant woman can also have appendicitis, gall-bladder disease or intestinal obstruction, all of which should be treated surgically, the fewer deaths there will be from surgical complications. Last year there were 5 deaths from appendicitis, 4 from idiopathic peritonitis, 1 from gall-bladder disease and 3 from intestinal obstruction. In all these cases, except those of idiopathic peritonitis, the deaths could have been prevented.

There were 7 deaths attributed to shock. As is generally recognized, many such cases can be cured by immediate and adequate transfusion.

There were 6 deaths listed as accidents of labor, namely rupture of the uterus, 5 spontaneous and 1 traumatic. Undoubtedly some of those listed as dying from shock actually had a ruptured uterus. We must remember that accouchement forcé is of historical interest only, when we learn that a physician used that method in dilating the cervix and delivered the patient by version, only to have her die three hours later, we can only think that the man, although perfectly honest himself, has not kept abreast of the times.

Twenty-three patients died following abortions. We cannot at present do much to help this situation.

There were 2 deaths from emboli in 1938. Unless such deaths are associated with unwarranted operative procedures they cannot be prevented.

There are still too many deaths due to albuminuria and eclampsia. There were 31 such deaths in 1938, in 11 of which the patient was undelivered. We know perfectly well that most of these deaths were preventable. Some of them were the result of the ignorance of the patient — there were two patients who had never seen a doctor until they appeared in the hospital, edematous and very ill. Some of the deaths were undoubtedly due to unintelligent procrastination by the physician.

earlier induction of labor would have prevented them

Hemorrhage was the cause of 26 deaths, and will continue to contribute largely to maternal mortality. We should be adequately prepared for intelligent transfusion by which is meant that all patients should be matched and cross-matched. There were 2 deaths apparently due to errors in typing.

Twenty patients died of pneumonia and 17 of cardiac disease. Pneumonia in pregnancy is a very serious complication and obstetricians who have

patients with pneumonia should secure the best possible medical consultant. The patient should be treated intelligently and adequately. Five of the patients who died of cardiac disease were undelivered, and 5 were delivered normally. It is a generally accepted maxim that if a woman dies of heart disease undelivered, she should never have been allowed to become pregnant in the first place.

This study is to continue for three years more. We need the full co-operation of every physician in the State, and we hope that this will be given us gladly and willingly.
330 Dartmouth Street.

RUPTURE OF THE UTERUS

FREDERICK J. LYNCH, M.D.*

BOSTON

RUPTURE of the uterus has occurred at the Boston City Hospital 33 times in the last 20 years. This incidence, it must be realized, is high because of the large number of complicated cases in which the patient was referred to the hospital after having been in labor for many hours. The 33 cases may be classified according to cause as shown in Table 1.

In this series 17 women died of a mortality of 53 per cent, and 29 babies, a mortality of 88 per cent. The rupture was treated by a supravaginal hyster-

ectomy. With each contraction of the uterus there is a slight taking up of the lower uterine segment, and this phenomenon lasts as long as the uterus continues to contract. The cervix is held securely in place by the sacral ligaments posteriorly by the broad ligaments laterally and by the round ligaments laterally and anteriorly. It is thus apparent that after the cervix is fully dilated, unless the contents of the uterus are moved forward in the birth canal the lower uterine segment becomes excessively thinned out, and if relief is not afforded rupture may supervene.

The causes of rupture may be classified as traumatic and non-traumatic. In the first group are included ruptures from external trauma as from a fall or blow internal podalic version as *couchement forcé*, the use of forceps through an incompletely dilated cervix and the manual removal of the placenta. The second group includes ruptures from dystocia scars from previous cesarean section, curettage, myomectomy, placenta previa and the injudicious use of pituitrin.

The rupture, again, may be either complete or incomplete. In the former type the peritoneum covering the uterus is included and there is communication with the abdominal cavity. The fetus is frequently extruded from the uterus and is found in the peritoneal cavity immediately beneath the examining fingers, while the uterus is found as a contracted organ at one side. If the baby has been delivered from below the examining hand may find in the vagina a loop of intestine or a portion of omentum. If these structures are not present it is usually possible to introduce the hand into the abdominal cavity.

In incomplete ruptures the tear involves the uterine musculature through the peritoneum but the abdominal cavity is not entered. A

TABLE 1 *Classification of Cases According to Cause*

CAUSE	NO OF CASES
Forceps failure and version	9
Previous cesarean section	6
Version	4
Spontaneous rupture	3
Prolonged labor (patient undelivered)	2
Manual removal of placenta	2
Low forceps	2
External trauma	1
Breech extraction	1
High forceps	1
Normal delivery	1
Total	33

ectomy in 21 cases with 11 deaths, a mortality of 52 per cent. In 4 cases a laparotomy was performed and the wound was sutured; of these patients 2 died. Eight cases were treated by vaginal pack with 5 deaths, a mortality of 63 per cent.

The mechanism of the dilatation of the cervix was first described by Bandl. He pointed out that in the uterus during the process of labor two distinct processes take place. The fundus contracts forcibly and the cervix dilates. The musculature is therefore divided into two entirely different segments—the upper or contracting and the lower or dilating.

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hematoma invariably forms at the site of the rupture, and the bleeding provoked by its disturbance on vaginal examination, added to the shock and the amount of blood already lost, is frequently enough to cause immediate death

TRAUMATIC RUPTURE

Forceps failure and version constituted the most frequent cause of ruptured uterus in our series. This sequence of events must be considered as having been due to an error in obstetric judgment. The fact that the head after many hours cannot be pulled through the pelvic brim is positive evidence that the patient should have been delivered by cesarean section. In many cases this should have been done after the patient had had a reasonable test of labor.

It is also true that most patients will deliver themselves if treated with intelligent expectancy. All obstetricians have encountered cases, perhaps well advanced in labor, in which a reasonable amount of traction with forceps has failed to advance the head. Version done in these cases is frequently successful. This satisfactory termination may be understood if we consider the head as being roughly triangular. When a forceps is applied to the vertex, one is trying to cause the base of the triangle to advance, whereas with version the apex of the triangle is applied to the pelvic inlet. In these poorly handled cases of disproportion it takes many hours of labor to dilate the cervix. One reason is that the membranes rupture early, another is that the disproportion between the head and the pelvis prevents the necessary application of the former to the cervix as a dilating agent. The prolonged labor results in the excessive thinning out of the lower uterine segment, and unless extreme caution is taken, rupture of the uterus may result even following the version.

The reprehensible dragging of a head with traction forceps through an undilated cervix is an obvious cause of rupture of the uterus. The use of forceps, even in cases in which the cervix is thought to be fully dilated, occasionally results in marked damage. If the lower uterine segment has thinned out to its greatest capacity, it is understandable that what would ordinarily result in a simple cervical tear might cause the splitting of the overstretched lower uterine segment. This condition may also be accounted for by the fact that until the head is on the perineum and in sight, complete retraction of the cervix has not taken place. With the application of forceps in the high or mid position, particularly if a slight rim of cervix is present, a forceful dilatation may also produce a tear which involves the lower uterine segment. Rarely, a tear which accompanies a normal delivery extends beyond the

cervix. This unfortunate accident occurred in one of our cases and resulted in the patient's death.

The unskillful introduction of forceps blades, the forceful rotation of the fetal head and the manipulation of destructive instruments for the removal of a dead fetus may also cause perforation of the uterine wall.

For many years it was agreed that if a patient had had a cesarean section all subsequent pregnancies should be terminated in the same manner. During the last decade this dictum has been somewhat modified. If the cesarean section was done on account of an abnormal pelvis or for a cardiac condition, it is obvious that the same indication exists in all subsequent pregnancies. If, however, a multiparous woman has had a cesarean section for an intercurrent indication, such as placenta previa or the separation of a normally implanted placenta, it is reasonable in a subsequent pregnancy to give her a trial at labor, provided this is done in a well-equipped maternity hospital. Labor may be permitted to continue as long as progress seems normal. If any evidence of trouble presents itself, such as an irregularly contracting uterus, a tender fundus, a rising maternal pulse or cessation of uterine contractions, a cesarean section should immediately be performed.

It is essential to realize in this connection that if the transient indication occurs in the first pregnancy, the patient should always be delivered by cesarean section. The important point is that this patient would have what amounts to a primiparous labor so far as her soft parts are concerned, and such a long and tedious labor should be avoided in the patient having a cesarean scar in the uterus.

In hospital practice, patients who have been delivered by cesarean section occasionally avoid hospitalization during the first stage of labor in an effort to escape a second operation. Frequently these women have some pelvic indication and expose themselves to the grave danger of a ruptured uterus.

The absence of cases of placenta previa from the present series may be explained by the fact that very few patients at the Boston City Hospital with this condition have been delivered other than by cesarean section during the last twenty years. In the few cases of delivery from below in which rupture may possibly have occurred, its presence may have been obscured by a diagnosis of postpartum hemorrhage. This condition was formerly responsible for many cases of rupture of the uterus—particularly so when the procedure adopted was the indefensible accouchement forcé. As a result of the placenta's being inserted in the lower uterine segment, in these cases the latter is

mely soft and friable. Any attempt at artificial dilatation results only in extensive tearing. This is also true when hydrostatic bags are used. After the expulsion of the largest bag cervical dilatation remains incomplete, and when the bag is drawn through the cervix following version, tears occur which frequently involve the entire uterine segment, with the production of a ruptured uterus.

My memory goes back to the days when a mechanical force was employed to terminate pregnancy in eclamptic patients. Although I never in actual use the instruments devised for dilatation of the cervix, I have seen several manual dilations of the cervix, followed by version and extraction. In the cases that terminated fatally although the cause of the death was given as toxemia and the "shock" of cervical dilatation, patients died, as all must realize, of unrecorded rupture of the uterus.

SPONTANEOUS RUPTURE

In the rare cases in which spontaneous rupture of the uterine wall has been weakened. The conditions which most commonly contribute to thinning are myomectomy, recent curettage, cancer and hydatidiform mole.

The removal of the placenta may result in a weakening of the uterine wall. Blows or falls may be the cause of a rupture. The trauma usually does damage to the uterine wall. Uterine rupture does not follow for some hours, and there may be surprisingly little in the way of signs or symptoms to give warning of its imminence.

I recall a patient who early in the first stage of labor suddenly began to show signs of difficulty. She was a normal multipara who had been followed in the prenatal clinic. Three days before delivery she had slipped on a wet floor and on falling struck her abdomen against a pail. This was followed by some abdominal pain and bearing down at full term and believing herself in labor she walked into the hospital. On entrance her age was 30 and the physical findings were those of any patient starting labor. She was observed for twenty-four hours in the labor room, and because the pains quieted down was sent to the ward. On the morning of the third day in the hospital she began to have pains again and was sent back to the labor room. Palpation of the abdomen showed clearly that the baby was free in the abdominal cavity and that a rupture of the uterus had occurred. Laparotomy was immediately performed. The baby was found half expelled from the uterus and tamponing a rent in the lower uterine segment, which involved the left broad ligament. When the baby was extracted the pressure on torn vessels was re-

leased, and a fatal hemorrhage occurred before hemostasis could be secured. This case is cited to demonstrate how slight the injury may be which results in a rupture of the uterus.

When posterior pituitary extract was first introduced its indiscriminate use was followed by many serious accidents. Although no such accidents occurred in this series, the danger accompanying the use of the drug should be repeatedly pointed out. Owing to the continued warnings of teachers of obstetrics during the last two decades this cause of ruptured uterus has been practically eliminated.

CONCLUSIONS

The treatment of rupture of the uterus is preventive. In a very large majority of the cases here reported this complication could have been anticipated. The avoidance of procedures which we have learned are frequently accompanied by serious trouble would have considerably lessened the occurrence of rupture of the uterus, the gravest of all obstetric accidents.

475 Commonwealth Avenue.

DISCUSSION

DR. CHARLES P. SELDON, Boston: Dr. Lynch has presented an analysis of 33 cases of rupture of the uterus treated at the Boston City Hospital. An equal number of cases were treated at the Boston Lying-in Hospital between January 1, 1916 and January 1, 1938, an incidence of 1 in every 1105 deliveries. Eighteen were traumatic, and 14 spontaneous. The incidence of rupture is increased by the injudicious use of pituitary extract during labor by manual dilatation of the cervix, by internal podalic version and by previous cesarean section.

An outstanding factor in the etiology of traumatic rupture is multiparity. Obesity, large babies, and perhaps other factors predispose to abnormalities of presentation and position and uterine inertia and cervical dystocia are commoner than in primiparas.

As Dr. Lynch has shown the sequence of events in the development of traumatic rupture may be quite characteristic. Because of prolonged labor, fetal distress or demands for relief from either the patient or her relatives the physician feels obligated to bring about delivery under unfavorable circumstances. He accordingly manually dilates the cervix and applies high forceps. Forceps failing he attempts internal podalic version. Due to previous rupture of the membranes with escape of amniotic fluid, spasticity from prolongation of the labor or irritability set up by repeated attempts at delivery the uterine musculature does not relax sufficiently for the baby to be turned easily. Rupture occurs in the thinned-out lower uterine segment.

Since repeated attempts at delivery make the uterine musculature increasingly spastic, craniotomy or a high-forceps operation should not be attempted if there is reasonable doubt of its success. If the operator believes that he can safely deliver the patient by internal podalic version he should proceed forthwith. Full surgical anesthesia with open ether is the anesthesia of choice. If the uterus cannot be relaxed under anesthesia, version should be abandoned and the patient delivered either by an extraperitoneal cesarean section or by a Porro hysterectomy.

Cesarean section is the most important predisposing cause of spontaneous rupture of the uterus. Twenty seven and three tenths per cent of all ruptures of the uterus treated at the Boston Lying in Hospital followed a previous cesarean operation, illustrating that this is not "just another way to have a baby." It was the predisposing factor in 64 per cent of the spontaneous ruptures. Fundal scars tend to rupture during pregnancy while scars in the lower uterine segment pull apart during labor. When the lower segment begins to develop during labor, a longitudinal scar in the lower segment is subjected to less stress than is a transverse scar.

Maternal mortality is influenced by the time interval

between rupture and the institution of treatment. Hysterectomy and adequate drainage of the peritoneal cavity performed within four hours of the occurrence of rupture give the best results. Expectancy has no place in the treatment of this condition. Patients with unrecognized or untreated ruptures die of infection if they do not succumb to hemorrhage and shock. There will be fewer unrecognized cases if the operator inserts his hand and carefully palpates the interior of the generative tract following each difficult delivery. Uterine tamponade is a valuable procedure for control of blood loss while preparations are being made for operation. Transfusion is an indispensable adjunct and may save the patient's life.

OBSTETRIC ANALGESIA AND ANESTHESIA

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THIS paper presents an attempt through a survey of the literature to consolidate opinion and to choose a drug or collection of drugs for obstetric use most suited for the average patient under average circumstances. An effort has been made to reflect the opinion of no particular group, but rather to correlate the findings of representative groups throughout the country.

The relief of labor pains has been of interest to medical men for many years. In 1847 Sir James Young Simpson, of Edinburgh, first used chloroform for this purpose.¹ With the development of ether, it was used considerably in obstetrics. In 1870 Alexander Simpson reported the first employment of opiates during the early stages of labor, their use for this purpose having been discovered by accident. For many years afterward the administration of opiates with the addition of ether or chloroform by inhalation was the procedure of choice for relieving labor pains. The development of these measures resulted in much lay and clerical discussion of the moral issues involved. In spite of adverse criticism progress continued, although slowly. Nitrous oxide was developed as an analgesic and anesthetic during labor in 1880, and early in the twentieth century it was brought to this country and thoroughly popularized. Following the introduction of spinal anesthesia in 1889, it was tried in obstetrics by several daring individuals.

Early in this century the use of morphine and scopolamine ("twilight sleep") was suggested by Steinbuechel followed by Krönig and Gauss. The clinical employment of this combination was observed in European clinics by various interested persons, following which it was introduced in this country. Its wide and indiscriminate adoption brought extensive condemnation over a period of

years, and the experimental work of Wallace in relation to the use of ether-oil rectal anesthesia was welcomed. Davis and Gwathmey put this experimental work to clinical use in the early 1920's, adding morphine and magnesium sulfate. This became the accepted procedure for the next few years.

In 1924, twenty years after the discovery of barbituric acid by Fischer and Dilthey, reports on the use of Sodium Amytal began to appear in the obstetrical literature. Since that time the literature on the barbiturate series has become extensive. In 1934 there was published a paper by Irving, Berman and Nelson² presenting a comprehensive clinical analysis of modern methods of obstetric analgesia and amnesia. This paper deserves particular mention in that it gives the most suitable and instructive approach to the subject that has yet appeared.

At the present time there are almost as many methods in general use as there are large obstetric clinics in this country. Gradually, valuable information is being compiled which will in the future materially alter methods now in vogue. What is primarily needed is a clearer understanding of pharmacology, pathology and applied physiology as related to these various drugs.

It seems proper to state that there is a small but active group of medical and lay persons who for medical and non-medical reasons deprecate the administration of any drug or combination of drugs in childbirth. These persons state that labor is a normal, essential experience and that failure or refusal to meet its attendant discomfort may result in serious damage to personality. They believe that no woman wants the birth of her baby to be a blank in her memory. They further contend that the pains of childbirth are very much overestimated, and that psychotherapy during the prenatal period can in a majority of

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prevent severe pain. Each obstetrician in his practice and experience must determine whether these contentions are worthy of more than a glancing notice.

The conclusion to be drawn from the sum of experience of a group of clinics is that the wide application of the principle of relief during labor presents a definite step forward. This statement is based not on the opinion of any group but on a study of mortality and morbidity statistics from clinics that have reported various methods of accomplishing this aim. The ardent opponents of the principle of relief have stated that babies are sacrificed to end pain. All available statistics on the subject indicate that the stillbirth and neonatal mortality have either not changed or have been substantially reduced during the years in which these drugs have been used. It is apparent that these drugs will continue to be employed with frequent modifications and improvements; it is not reasonable to expect that with a clearer understanding of their dangers and limitations further reductions in mortality rates may be brought about.

It is impossible to discuss fully the advantages and limitations of any drug or group of drugs except in relation to the anesthesia which follows. Anesthesia, if wisely chosen or improperly administered, may in a few moments bring about an unnecessary and entirely unforeseen result. In the past much attention has been paid to analgesia and amnesia and very little to anesthesia.

When we consider the sum total of drugs used for narcosis or anesthesia, can we state the end results that we may expect to obtain?

Our clinical experience over a period of years has brought out several facts of considerable value in relation to the administration of drugs during labor. These concern both the infant and the mother, and must be carefully considered in the evaluation of a suitable modern method of medication.

Opium derivatives are deservedly finding a narrower range of value. Their untoward effect on the respiratory center of the fetus is receiving wide recognition, with the equally satisfactory results obtained from other drugs, the employment of opium has become largely unnecessary. The chief advocates of morphine at the present time utilize small doses in order to fortify the action of barbiturates.

The increased use of paraldehyde is apparently a distinct advance, particularly when it is administered in combination with other drugs. Reports indicate a degree of safety not commonly found

in some of the other drugs frequently used. The marked tendency of this drug to prolong labor should be remembered.^{3, 4} Paraldehyde easily and quickly passes the placenta, but the effect on the fetus is not a serious one.⁵

Recently, various drugs, particularly of the barbiturate group, have been administered intravenously both during the course of labor and for terminal anesthesia at the time of delivery. These drugs are distinctly more toxic than similar drugs given by other routes. Anesthetics intravenously administered are contraindicated when a patient has previously received even moderately large doses of other drugs. The marked depressant effect of these drugs when used for terminal anesthesia makes them unsuitable for elective use at the present time.

Avertin is a dangerous drug. It should never be employed except by an expert anesthetist entirely familiar with its limitations. Its major drawback is its profoundly depressant action on the respiratory center; in this respect it is even more dangerous than chloroform.⁶ In doses of over 5 mg per kilogram of body weight it may produce uterine atony with resultant postpartum hemorrhage. Inasmuch as the depth of narcosis depends on the rate of absorption rather than on the amount given, individual variations are marked and dangerously deep narcosis may result from a moderate dose. Avertin has no place in obstetrics.

The barbiturate series is the most widely used group of drugs in modern obstetrics. It is probable that this popularity is deserved. Reports are numerous, results in different clinics are comparable, and contraindications and limitations are gradually receiving a proper amount of consideration.

Pentobarbital and Sodium Amytal are the members of this group most widely adopted, the former being by far the most popular. These drugs are most commonly given in combination with drugs of other groups; they pass the placenta with ease and affect the fetus. Individual susceptibility varies widely and moderately toxic doses are fairly common. When they are given by mouth, respirations are decreased in rate and amplitude as the dose is increased, owing to a direct effect on the respiratory center. Contractions of the parturient uterus are not affected by doses causing complete analgesia.⁷

In employing the barbiturates it is important to give a small initial dose in order to determine idiosyncrasy to this group. Massive single doses are not only unnecessary but decidedly dangerous. The proper dose is the least amount that will give the desired result. This depends directly on the experience of the obstetrician and on the constant observation of the patient in labor. No rules as

to dosage can be given, either in relation to the weight or the age of the patient. Patients who are not good anesthetic risks should not be subjected to prolonged narcosis and depression. Pulmonary complications and the recent ingestion of food are contraindications. It must be remembered that their employment is always a matter of election and not of necessity.

There can be no doubt that babies as well as mothers are affected by the medication. This effect is determined by the size of the dose, the time of administration and the susceptibility of the baby, whether full term or premature. It is probable that the barbiturates should be administered with considerable care in the management of premature labor.⁸ In the average case the effect on the baby, although present, is not detrimental to its welfare. All studies indicate that since these and similar drugs came into general use stillbirth and neonatal death rates have remained the same or have been substantially reduced.⁸⁻¹⁰

The occurrence of pulmonary edema is a distressing effect of this group of drugs in an occasional case.¹¹ Reports of this complication are very rare in the literature, but the general impression is that it occurs often enough to be of great importance. This type of pathologic change is commonly found in animals following large doses, and its occurrence in the human subject following relatively small doses is probably associated with idiosyncrasy. The role of partially obstructed breathing in the causation of pulmonary edema has been reported by a number of observers. In dogs anesthetized with sodium barbital Moore and Binger¹² found no lung changes following obstruction to expiration, but obstruction to inspiration characteristically produced congestion and edema of the lungs. It is probable that this effect is due to the interference with a free airway rather than to any specific effect of the drug. Observations of this nature are of great clinical significance, and may well partially explain the occurrence of these signs and symptoms in patients receiving barbiturates. It is almost a universal finding that patients showing pulmonary edema have also "swallowed their tongues." It is obviously necessary to maintain a free airway in all persons under the effect of the barbiturates. The constant attendance of a responsible, experienced person is imperative.

Such pulmonary complications do not mean that these drugs are too dangerous for general adoption. They do indicate that cases must be individualized and that supervision must be strict. Their occurrence will be lowest in those cases where their possibility is borne in mind and proper measures are instituted for their prevention. It is certain that these drugs, in large doses, have in the past

been indiscriminately used by those unfamiliar with their pharmacologic action and toxic manifestations. This does not mean, however, that their employment increases the patient's risk in properly selected cases.

The amnesic action of scopolamine is made use of in most drug combinations. The incidence of successful results from the mother's point of view is very much lowered in those cases in which it is not used.² Relatively small doses at infrequent intervals are all that is necessary. Sensitivity to this drug is common, and initial doses should be small in order to determine the patient's reaction. If an untoward reaction occurs, the dose should not be repeated. Several papers have appeared attributing an increased incidence of puerperal psychosis and insanity to the use of scopolamine. The experience of most clinics has not borne out this contention.

The large majority of patients receiving drugs during the course of labor also receive some type of anesthesia at the time of delivery. The choice of an anesthetic for this purpose has not gained the attention it deserves, in addition to the usual indications and contraindications for anesthesia, we must consider its effect on the fetus. This appears doubly significant when we realize that the infant will be born at a time when the depressant factor is at its height, and under the direct effect of any anoxemia that may be present. We are faced with what amounts to a choice of anesthesia for the infant. Deep surgical anesthesia and any degree of anoxemia must be avoided whenever possible. Improperly administered anesthesia in all probability accounts for more slow births than does the character of the drugs given during labor. The value of minimal anesthesia during premature childbirth is well known. It is equally important in every full-term delivery.

The well-known dangers of chloroform do not require discussion. The consensus is that the drug has no place in obstetrics.

Cyclopropane has certain theoretical advantages, but requires special equipment and the services of a highly trained anesthetist. It is being widely used in several obstetric clinics at the present time, final judgment concerning this gas must await future developments.

Ether has a wide range of safety and usefulness. A minimum of equipment is necessary for its administration. Its chief disadvantages are the difficulties attendant on induction and the unpleasant nausea and vomiting which so frequently follow its administration. When given in full anesthetic doses its depressant effect on the fetus is frequently evident. It is most commonly used in combination with nitrous oxide for terminal

anesthesia Ether in oil is frequently given rectally during the course of labor. Its greatest value when so used lies in combating the restlessness following the administration of other drugs. It is best administered in repeated small doses, all ways remembering that large doses given rectally late in labor are very likely to affect the fetus.

In this country nitrous oxide enjoys great popularity not only as an agent for terminal anesthesia but also to enforce the action of various drugs during labor. When properly administered it is probably the most satisfactory agent for obstetric anesthesia now known, when improperly given it is exceedingly dangerous for both mother and child. Its untoward effects are entirely due to asphyxia resulting from faulty administration. Owing to its low potency it is frequently given with minimal amounts of oxygen. In many patients it is impossible to obtain proper anesthesia and still supply sufficient oxygen to prevent cyanosis. In the presence of anemia, severe anoxemia may be present before cyanosis is easily visible. For this reason anesthesia should never be given without a knowledge of the hemoglobin value, nor should this gas ever be administered without oxygen even for short periods during labor pains.¹³ When we consider the manner in which this gas is commonly employed by untrained persons, it is surprising that its results have been as good as those reported.

Several papers have recently appeared in the literature concerning the irreparable damage to the central nervous system resulting from insufficient oxygen concentrations during the course of nitrous oxide anesthesia.¹⁴ If these changes can occur in the fully developed nervous system of the adult, how much more serious damage may we expect to see in the undeveloped central nervous system of the newborn or unborn infant. Eastman¹⁵ has concluded that, when given in concentrations of 90 per cent or stronger over periods exceeding five minutes marked degrees of fetal anoxemia are produced in about one baby out of three, and occasionally profound asphyxia neonatorum results. It is fair to conclude that nitrous oxide and oxygen mixtures should always contain 15 to 20 per cent of oxygen.

It is quite probable that certain cases of fetal asphyxia, formerly considered due to the use of drugs during labor, are the direct result of improperly chosen or poorly administered anesthetics. Furthermore, obstetric anesthesia should be given only by those trained in its use and familiar with the pharmacologic action of the agents employed. With an understanding of the physiology of labor and the pharmacology of various groups of drugs, let us outline the management of a hypothetical case during labor. We shall presume

that our patient is a normal primipara without intercurrent disease, whose delivery is to be effected in a well-equipped hospital under the supervision of one qualified by training and experience to make obstetric decisions. For use during labor we shall choose that group of drugs combining, in the opinion of a majority of practicing obstetricians, the all-important virtues of efficiency and safety, when judiciously employed. These drugs will be Pentobarbital and scopolamine, with the addition of small rectal doses of either paraldehyde or ether if indicated. Terminal anesthesia will consist of a nitrous oxide, oxygen and ether mixture, given with a minimal oxygen content of 15 to 20 per cent.

Our patient will have received small doses of Pentobarbital several times during the prenatal period in an attempt to determine any marked idiosyncrasy. If she has followed our instructions she will not have eaten anything following the initial occurrence of labor pains. The patient will be sent to the hospital as early in labor as possible. In addition to the usual preparations a red cell count and a hemoglobin determination will be done routinely. If time permits several enemas will be given. Thorough cleansing of the lower bowel is essential, not only to ensure a clean field at the time of delivery but also to facilitate the absorption of any rectal medication.

The patient will be told that she can have the medication as soon as she feels uncomfortable as a result of contractions. Most patients want nothing until they are having regular contractions of moderate severity. The initial dose of Pentobarbital will be $4\frac{1}{2}$ to 6 gr., depending on the weight of the patient. This will be given in capsules by mouth and will be accompanied by 1/150 gr. of scopolamine, given hypodermically. The patient will at once be placed in a quiet, darkened room with a competent attendant who will remain with her until she has roused following delivery. In the absence of assistance of this sort, the patient will of necessity be denied medication. The attendant will not, without relief leave the patient's side for any reason whatever. She will at frequent intervals determine and chart the frequency, duration and severity of uterine contractions as well as the fetal heart rate. The attending physician will check these determinations at times, and will remain in constant touch with the progress of labor. No one should ask or expect nursing attendants, no matter how well trained to assume responsibility for the management of a patient under medication.

One hour following the initial medication in other dose of Pentobarbital may be given depending on the patient's condition. A maximum of 3 gr. is usually all that is necessary; this will be

given by rectum, the capsules being punctured with a needle to facilitate absorption. Another dose of scopolamine will be given at this time, 1/200 gr. If marked flushing or a distinct rise in pulse rate followed the initial dose, the second dose will be omitted. It will rarely be necessary or advisable to give further doses.

From this time on, Pentobarbital will be given only in 1½-gr doses and only on indication. The total dose during labor should in all probability not exceed 10½ gr.

The attendant will be instructed or will have learned from experience to restrain the patient as little as possible. Undue restraint only adds to the restlessness and is distinctly to the patient's disadvantage. If marked restlessness occurs, as it well may, it will become advisable to make use of paraldehyde or ether given by rectum. It is better to use small doses repeatedly than one large dose. The recommended dosage for paraldehyde is 8 to 16 cc, and for ether 60 cc. If delivery is imminent at the time the indication for further medication arises, the use of nitrous oxide and oxygen during contractions will probably be preferable. By this means the late depressant effect of the former drugs on the fetus can be completely avoided.

When the patient is ready for delivery, anesthesia will be started while the obstetrician is scrubbing. A nitrous oxide and oxygen mixture will be used, with the addition of what ether is necessary. No attempt will be made to increase the depth of anesthesia by reducing the concentration of oxygen. The amount and depth of anesthesia will vary widely with the type of obstetric procedure contemplated, the patient will be kept as light as possible until the birth of the baby. The choice of an anesthetist is an important one, as a fine degree of co-operation is necessary between him and the obstetrician. An expert surgical anesthetist is not necessarily well equipped for obstetric work until such a time as, through training and experience, he has become familiar with the peculiar problems involved. The choice of anesthesia will at all times be determined by the obstetrician.

In conclusion, we may prophesy that in the future new drugs designed to solve a majority of our obstetric problems will appear on the market. Similar drugs have appeared from time to time in the past, some of them well recommended. The small obstetric hospital or the small obstetric unit in a general hospital will best perform its function not by pioneering in the field of obstetric analgesia and anesthesia, but rather by making use of well tried and comparatively safe methods.

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DISCUSSION

DR GEORGE M SHIPTON, Pittsfield. I think it is very timely that we should have a paper presented before the section on this subject just now. The lay magazines are so filled with the marvelous stories of painless labor that our patients are beginning to come in expecting to be presented with a capsule on Tuesday and a baby on Thursday and know that it was delivered on Wednesday. In order to compete with this situation some obstetricians are promising their patients 100 per cent analgesia and attempting by various means to fulfill that promise. I think that we should in all fairness tell our patients that we wish to do all that we can to ease their stress of labor, that we can accomplish more if they arrive at the hospital early, but that we cannot promise 100 per cent success. We are having an occasional disaster to mother or baby as a result of too strenuous pushing of some of the analgesics.

A word about paraldehyde. I was glad that Dr Cornwall reassured that paraldehyde delays labor. You will remember that the early advocates of this drug insisted that it did not delay labor. There again, we may safely explain to our patients that they are going to receive a preparation which may delay labor as long as 50 per cent, but that an eighteen hour comfortable labor is preferable to a twelve hour labor without an analgesic.

In addition to delaying labor, paraldehyde is likely to cause a distended bladder, and we must be on the lookout for this complication.

We have had such good success with Pentobarbital, scopolamine, paraldehyde and nitrous oxide, with the technique outlined by Dr Cornwall, that we are justified in saying that our methods are improving. Nitrous oxide is, I believe, a very valuable analgesic, particularly at the termination of labor and as regards the newborn baby. This combination can be used successfully either for delivery or as the anesthesia and analgesic in cesarean section. And the minute the baby is born in either procedure the patient may be flooded with oxygen. This oxygen permeates rapidly, and the baby even before taking respiratory motion gains color. The amount of oxygen given is not enough to interrupt the anesthesia of the mother and cause her any difficulty, and I feel confident that it has saved a great many babies in the delay before respiration is started.

I congratulate Dr Cornwall on his thorough survey of the situation and his very fair evaluation of the various methods.

RUPTURE OF THE LIVER

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INJURY to the liver is the commonest of all injuries to the solid organs of the abdomen. At the Boston City Hospital between 1915 and 1937 there have been 60 such cases. Thorlakson and Hay¹ state that at the Winnipeg Hospital there were 10 cases in twenty years out of 200,000 admissions, and that of 3900 accident cases only 3 were those of rupture of the liver. Edler² found that in 365 cases of injury to solid organs the liver was involved in 50 per cent. Rupture of the liver, however, is one of the rarest reported surgical emergencies. The importance of a thorough study of this condition lies in the absolute necessity of early diagnosis and operative intervention in order to control hemorrhage and circumvent infection.

Rupture of the liver is most commonly due to violent injuries, yet seemingly trivial injuries may cause a laceration, as demonstrated by a case at the Boston City Hospital of a nine-year-old boy who ruptured his liver by falling on the edge of a curb. Sudden blows on the trunk are the most frequent cause of this condition regardless of the source of the blow. It is almost certain that a fall from any extreme height will produce a lesion of some degree in the liver.

It is absolutely essential to recognize rupture of the liver early in order that proper care may be instituted promptly. Thölle³ states that the mortality increases from 2 to 5 per cent with each hour's delay in treatment. Our statistics confirm this assertion. Spontaneous hemostasis is rare in the liver because the blood vessels are without valves, are thin walled and do not retract or contract after sectioning, and because blood mixed with bile coagulates slowly. Although the liver apparently destroys a certain number of pathogenic bacteria delivered to it by the portal system, this condition does not hold true when it is traumatized and in the presence of blood the same bacteria may and usually do produce severe infections. Martin and Trusler⁴ have demonstrated that bacteria found in the livers of normal adult dogs rapidly produce toxic amines in the process of incubation *in vitro* and believe that the reaction associated with the absorption of putrefactive amines and other split protein products formed by bacterial action on the liver protein *in vivo* explains the shock syndrome associated with such infection in the human subject. In addition Boyce and McFetridge⁵ have shown that autolysis of liver tissue *in vivo*

has a clinical aspect with regard to so-called liver death. Aseptic implantation of whole and ground liver into the peritoneal cavity of dogs produced death in eight to eighteen hours and each dog presented characteristic autolytic peritonitis. When the ground liver was autoclaved before implantation death was delayed for thirty-six hours. These authors believe that death is due to the absorption of toxic products generated from the liver tissue deprived of its circulation. The role of the gas bacillus in autolytic peritonitis they deem entirely secondary, the autolysis of the liver tissue producing the fatal results. In their studies the anaerobic organism was always present in the cultured peritoneal fluid, regardless of whether or not the liver had been autoclaved. Yet the injecting of the peritoneal fluid either intravenously or intraperitoneally failed to produce the picture of autolytic peritonitis. Boyce and McFetridge maintain that the gas bacillus acts as a catalytic agent and merely hastens the autolysis. Their work is of clinical importance in emphasizing the necessity of early exploration in every case in which injury to the liver is suspected. It also indicates the best method of treating such injuries. These authors declare that abrasions should not be touched, that lacerations should be sutured and not packed, and that where there is extensive lysis of liver tissue, resection of that part is the best treatment.

The liver is the largest internal organ of the body and by far the largest glandular organ. In the normal state it is almost entirely protected by bony structure. It is supported from the diaphragm by the ligamentum falciforme hepatis and the ligamentum coronarium hepatis (Fig. 1). The peritoneum does not cover the posterior surface of the right lobe, but Glisson's capsule here comes into direct union with the fascia of the diaphragm. The inferior vena cava is a supporting structure for the liver because this vessel is firmly fixed to it and to the orifice where it passes behind the diaphragm (Fig. 2). The ligamentum falciforme hepatis is of little aid in supporting the liver for it is a loose fold of peritoneum through which passes the umbilical vein during fetal life. This structure is later obliterated to form the ligamentum teres. The falciform ligament also carries accessory portal veins and lymphatic vessels which connect with the internal mammary vessels. These vessels come into prominence in portal obstruction when it is necessary for collateral circulation to develop.

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POSITION AND INCIDENCE OF INJURY

The right lobe is involved much more frequently (in 95 per cent of cases) than is the left, chiefly because of its larger size. Its anterior and posterior surfaces are in direct contact with the abdominal wall and receive the full impact of

supporting tissue in the young is more elastic than that in the old, but not so abundant, and the parenchymal tissue in the young is therefore less firmly supported. Not a single case in the present series showed cirrhosis. Livers in the young have been torn much more frequently in

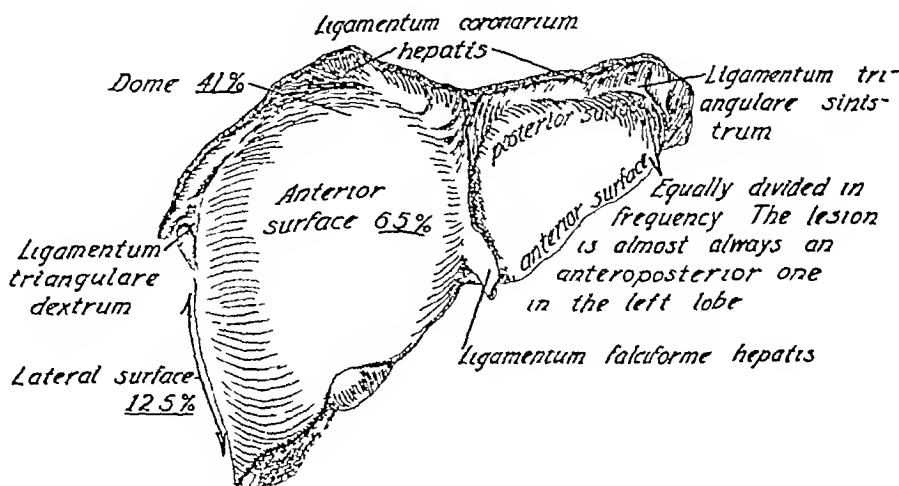


FIGURE 1

a blow. Of the 60 cases reviewed, involvement of the left lobe occurred in only 3. However, Branch⁶ reports 1 case in which the left lobe was completely detached from the right and the patient made a good recovery following its removal. The positions of the injuries were those given in Figures 1 and 2.

a stellate direction, and the livers of older patients have shown a tendency to tear in a more or less straight line. There are two other factors influencing the direction of the laceration, both having to do with the force rupturing the liver. When a compression force is applied, the liver tears in an anteroposterior direction. When

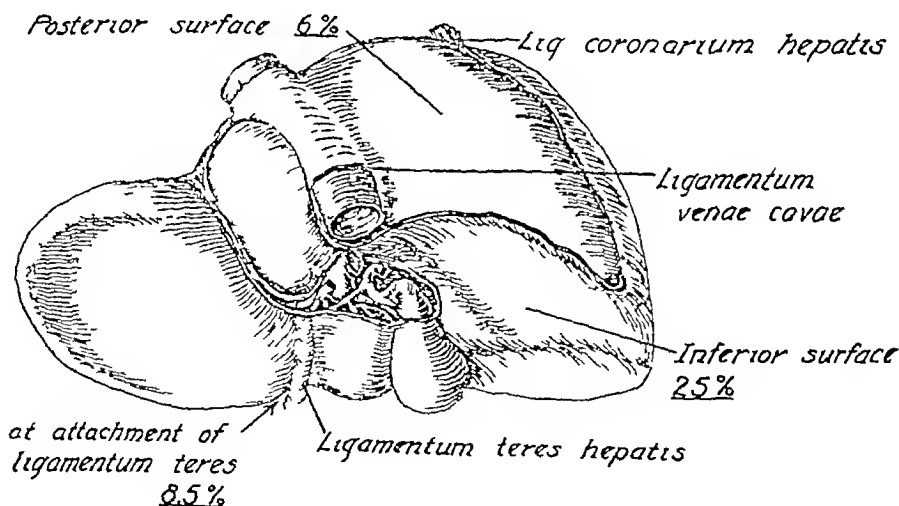


FIGURE 2

Chart 1, rupture of the liver is frequent in young people than in old. This can be accounted for on the basis of the fact alone, for the young engage in more vigorous activities than do the old. It is that the bony protection in the young is more supple and that minor blows are likely to reach the liver. The

a flexion force such as would jackknife the body is applied, the direction of the tear is usually transverse. Another significant observation is that liver ruptures in the young are frequently on the inferior surface near the hilus or at the site of attachment of the obliterated umbilical vein (ligamentum teres). The dome of the liver is the part most often ruptured in the older age groups.

u. ch these struc- tulation
1 Bushi
2 Irving
hypnotic

CLASSIFICATION OF INJURIES

Moinihan's classification of rupture of the liver is the simplest and most satisfactory. He gives three degrees: rupture of liver tissue with laceration of Glisson's capsule, separation of the capsule with subcapsular hemorrhage and central rupture leading to hematoma and thence to abscess or cyst. Spontaneous rupture should be added to the above classification in order to make it more complete. Spontaneous rupture is almost always secondary to syphilis or carcinoma of the liver. A case due to malaria has been reported (McEwan and McEwan³). Mazel² explains that in traumatic lesions the rupture is the

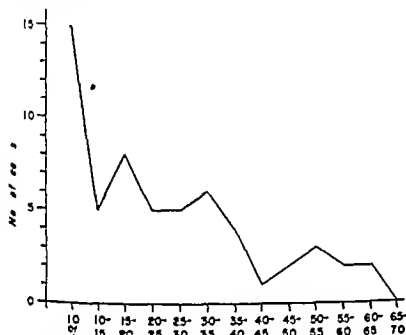


CHART 1. Incidence of Ruptured Liver According to Age

cause of the hemorrhage, while in spontaneous rupture the hemorrhage is the cause of the rupture.

SEX AND ETIOLOGY

The ratio of male to female patients in this series was 5:1. Every one of the women had sustained injury as a result of an automobile accident. Although the men had been injured in all sorts of accidents, most of the injuries had been produced in one way or another by an automobile. One child fell while walking the curbing and struck his right lower ribs. Another was kicked in the chest into a tree. Another was kicked in the side by a horse. A few were injured while playing games, chiefly football. The wheel of some vehicle traversing the abdomen was a common cause of injury. Falling from a height of two stories was the etiologic factor in 3 cases and falling from a greater height in many others. There was only 1 case of gunshot wound.

CONDITION OF PATIENTS ON ADMISSION

Seventy-five per cent of the patients were brought to the hospital immediately following the accident. The longest delay in reaching the hos-

pital was sixty hours. Eighty per cent of the patients were in shock on arrival, and it was necessary to combat this condition before operative treatment could be instituted.

PHYSICAL EXAMINATION AND DIAGNOSIS

Physical examination of a typical case of rupture of the liver revealed a patient with a fast pulse, subnormal temperature, cold moist skin, pallor, rapid shallow breathing and pain throughout the abdomen with the greatest tenderness in the right upper quadrant. Laboratory findings were not significant except for the white-blood-cell count, which was high, varying from 13,000 to 28,000. Repeated blood counts which show a progressive fall in the red blood cells and a constant rise in leukocytes are indicative of loss of blood into a serous cavity. The work of Wright and Livingston¹⁰ is interesting in this connection. They have shown that in cases of internal hemorrhage leukocytosis occurs only if bleeding takes place in serous cavities, the rise occurring promptly and reaching a maximum in five or six hours.

An exact diagnosis cannot be made except on exploration, but the need of immediate laparotomy can be shown without great difficulty. Given a patient who has met with a blow to the mid-trunk and soon shows signs of shock, together with tenderness in the right upper quadrant, rebound tenderness (blood in the peritoneal cavity) and an elevated white-cell count (bleeding in a serous cavity) an exploration is mandatory.

TREATMENT OF SHOCK

Usually the patient stands the shock well and responds quickly to treatment. It is wise to take enough time to prepare him for operation. In this respect rupture of the liver differs from rupture of the spleen. A ruptured spleen is likely to exsanguinate the patient more quickly than is a ruptured liver. This is because the splenic artery is a large vessel with high pressure, so that if a main branch is severed bleeding is profuse. Furthermore, bleeding into the fragile splenic tissue may result in a great increase in pressure and a consequent enlarging of the original rent. Shock should be treated immediately by all the means in one's possession. Because the use of large transfusions is important, it is essential to obtain proper donors at the earliest moment. The patient should receive whole blood before, during and after the operation in sufficient quantities to keep the blood pressure within the range of safety, usually considered to be between 90 and 100 mm. of mercury systolic. The patient should be treated for his shock on the operating floor, and if possible on the operating table so that movement may be re-

duced to a minimum. Even the slight movement of the abdomen required in transferring the patient from the litter to the operating table may produce further tearing of the liver or dislodge a protecting clot.

COMPLICATIONS

In considering the complications of rupture of the liver the patients in this series are divided into two groups: those who died (41 cases) and those who survived (19 cases). In the latter the complications were fractures in 8 cases (ribs, 3, vertebrae, 2, femur, 3), contusions and abrasions in 16 and ruptures in 6 (gall bladder, 1, tear of mesentery, 3, pneumothorax, 1, hemothorax, 1). Postoperatively 40 per cent of the patients drained bile from their wounds, but in all cases drainage ceased by the twelfth day. Among the patients who died the concomitant injuries were fractures in 14 cases (skull, 9, ribs, 3, vertebrae, 2) and other ruptured viscera in 17 (spleen, 7, bladder, 2, esophagus, 1, kidney, 4, lung, 2, gall bladder, 1). In most cases death occurred early, that is in the first twelve hours after injury. It is thus obvious that patients with serious complicating injuries such as rupture of the spleen, diaphragm or esophagus have much less chance of surviving than those without. The most serious factor contributing to the high mortality was the extent of the lesion. Hemothorax, rupture of the diaphragm, spleen and hollow viscera and rupture of the lung were the factors which determined whether the patient was to die quickly of shock or hemorrhage, or succumb a few days later to pneumonia or other complications.

MORTALITY

Twenty-six patients died before operation could be performed. Of the 34 operated on, 15 died and 19 recovered, a mortality rate of 44 per cent. The mortality rate, however, for the entire series of 60 cases is 68 per cent. Twenty-five patients died in six hours or less after being admitted to the hospital, only 12 died after the first twenty-four hours in the hospital. Deaver and Ashhurst¹¹ give the mortality rate of their unoperated cases as 80 per cent, and that of their operated ones as 60 per cent.

METHOD OF REPAIR

Good exposure is absolutely necessary in the repair of all ruptured viscera. In thin patients any incision used will give good exposure, but in the barrel-chested it is wiser to limit the incision to a transverse one. The incision may be extended all the way across the abdomen if injury to the spleen or other left-sided organs necessitates it. The ideal to be attained in repair of the liver is

the control of hemorrhage and the circumvention of infection. Immediate control of hemorrhage is easily accomplished by digital pressure on the portal vein at the foramen of Winslow. Many surgical methods for the permanent control of hemorrhage have been advocated such as the use of compression clamps (Clementi¹²), cautery (Ullmann¹³), packing with various materials such as gauze, muscle (Beck¹⁴), omentum, contiguous organs, fat, fascia and rubber dam, ligature carried on a blunt, non-cutting supple needle such as that used by Kousnetzoff and Pensky¹⁵, and ligature with various materials including silk, catgut and fascial strips. The use of steam is advocated by Snegirew¹⁶, that of decalcified bone plates on the upper and under surfaces of the liver is recommended by Ceccherelli and Bianchi¹⁷. The simplest method that will check hemorrhage is the best. Gentle packing with gauze is the quickest and easiest, but not always the wisest, procedure. There are occasions when large vessels may be tied separately and the liver tissue pulled together by catgut sutures without drainage. In areas inaccessible to the needle, such as the posterior surface, gentle packing is the best method of controlling hemorrhage. Occasionally it is necessary to employ muscle as the hemostatic material. This is easily procured, and can be used with one pedicle still attached. If no nonabsorbable material is used as a tampon the wound may be closed without drainage, even though large areas of liver tissue have been exposed.

To circumvent infection is the next purpose of the operation for injury to the liver. All loose fragments of tissue deprived of blood supply must be removed, for should they remain, autolytic peritonitis is very likely to supervene. A gauze drain left at the site of injury should be removed on the third or fourth day at the latest, unless there is marked infected drainage at this time, in which case the drains should be left for five or six days more. Bile drains in 50 per cent of cases, but this of itself rarely causes harm.

CARE OF COMPLICATIONS

Critical judgment is required in caring for the complications occurring with rupture of the liver. Other injuries to the abdominal organs must be suspected even though a ruptured liver is found. Any blow severe enough to produce one can cause other injuries. Gastric suction by the Wangensteen method is imperative, in our opinion, in all cases of abdominal injury where distention, nausea or vomiting is present or is at least possible, which is nearly always the case. It should be employed before and during operation, and for several days postoperatively until normal peristalsis has oc-

curred. The injuries demanding immediate attention include fractured vertebrae, which must be cared for according to the established methods of support and for the prevention of cord injuries. Ruptured spleens must be removed immediately, and demand the surgeon's first attention. Ruptures of the gastrointestinal tract must be suspected and when found sutured. Ruptured bladders must be sutured and placed on constant catheter drainage, with drainage of the space of Retzius. Ruptured gall bladders may be drained or removed.

CARE OF POSTOPERATIVE COMPLICATIONS

A patient failing to improve after operation should be suspected of harboring an abscess, particularly around the liver and occasionally within it. X-ray examination affords the best check on this condition. Peritonitis is the commonest postoperative condition, and is treated in the usual manner by absolute quiet, intravenous administration of fluids, adoption of Fowler's position, in brief by Ochsnerizing the patient. If the patient survives it is certain that he will have no complaints so far as his liver is concerned even though considerable liver substance has been removed. Ponfick¹¹ stated in 1890 that animals could survive with only one eighth of their liver tissue remaining. However, should the blood supply to the liver be destroyed death ensues very quickly.

SUMMARY AND CONCLUSIONS

A series of 60 cases of rupture of the liver is reported.

The gross mortality rate in the series was 68 per cent, and the operative mortality rate 44 per cent.

Suspected ruptured viscera cases should be operated on early, since the mortality rises rapidly with each hour's delay.

It is doubtful whether patients with ruptured livers surviving three days or longer should be operated on.

The presence of an elevated leukocyte count and a falling red-cell count is indicative of bleeding into a serous cavity.

All loose fragments of liver deprived of blood supply should be removed.

The commonest postoperative complications are in the order of frequency peritonitis, postoperative hemorrhage, subdiaphragmatic abscess, intrahepatic abscess, subhepatic abscess and abscess of the lesser peritoneal cavity.

Except for exposure no type of incision possesses any special advantage. Transverse incision gives a better exposure in barrel-chested patients but is of doubtful advantage in thin patients.

Infection after liver injury is common.

Drainage of bile occurs in 50 per cent of cases but ceases in every case by the third week.

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REPORT ON MEDICAL PROGRESS

TRAUMATIC SURGERY

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IN DISCUSSING the recent advances in the surgery of trauma, it is not so necessary to describe new developments as it is to restate old surgical principles and realign them in the order of their importance. I shall discuss the treatment of burns, the treatment of wounds, the treatment of wringer hands and the injection treatment of hernias.

TREATMENT OF BURNS

The treatment of burns has been discussed in medical literature since the days of Confucius, who used tannic acid in the form of tea, and since the writings of Hippocrates, who used ointment of beeswax and balsam. Even more important than the local care of the burn is the general treatment of the patient. The care of a severely burned patient should consist in treatment of shock and relief of pain, the prevention of blood concentration and local treatment of the burned area.

Shock, with poor pulse, lowered blood pressure and loss of body heat, must be treated by warmth (heaters and blankets) and intravenous fluids, the pain must be allayed by sufficient morphine. Following thermal trauma, there is a great outflowing into the burned area of serum from the tissues and blood stream. This causes a loss of blood plasma and a concentration of cells in the circulating blood, indicated by a sharp increase of the red blood-cell count. If the plasma loss continues there follow grave physiologic changes ending in respiratory and cardiac failure. In this way a vicious cycle is established and the patient finally dies in collapse. In order to prevent this the patient must be furnished with adequate fluids, either intravenously or by mouth. The red-cell count must be kept at a normal level. Blood transfusions are necessary so as to supply the patient with adequate plasma. All these measures must both precede and accompany the local treatment. It is the pain, shock and loss of plasma that kill the patient rather than the burn itself. Therefore we must direct our attention first to the care of the patient rather than to the local treatment.

The two ancient methods of local treatment are still in common use. The first is the tannic

acid method. The burned skin is covered with a freshly made 10 per cent solution of tannic acid in water. This treatment must be continued until the burned skin is thoroughly and completely tanned. In extensive burns it may be necessary to immerse the patient in a tub of warm tannic acid solution, later drying him with a hot-air dryer and returning him to a warm bed in which he is protected by cradles. It may be necessary to re-tan the rim of the eschar.

The second method is the occlusive one. In this the whole burned area is closed with an elastic seal of cod-liver oil ointment or paraffin, held firmly in place with splints. The warm paraffin wax is sprayed on with a special atomizer. These dressings can be done with little pain. The adjacent skin must be kept scrupulously clean in order to prevent external infection. If infection occurs, daily dressings of paraffin wax seem to be the least painful method. After the eschar separates, the clean granulating surface should be promptly covered by razor skin grafts. This method gives a strong and satisfactory skin covering. Reconstructive measures for scars and contractures may be done later. The general condition of the patient as outlined above must be carefully and continuously followed until healing is complete.

TREATMENT OF WOUNDS

Formerly much emphasis was laid on the effectiveness of strong and sometimes colorful antiseptics for sterilizing wounds. It is true that these chemicals destroy bacteria, but at the same time they cause cell changes and even the death of tissues. They hinder rather than help healing. Now simple ancient surgical principles have again come to the fore in the following order: protection, cleansing, repair, dressing and splinting.

Protection

The first-aid treatment should be simple. A sterile protective dressing should be applied and held in place by a bandage under moderate pressure. A splint is often necessary. All efforts to stop bleeding with instruments or to investigate the depth of the wound, or to pour antiseptics of any kind into it, should be discouraged. Clinical

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evidence has shown that the dirt carried into a wound at the time of injury is usually less apt to cause serious infection than unsterilized instruments, dirty fingers or other materials used in hasty and ill-considered efforts at first aid.

Cleansing

In the hospital, sedatives should be given to relieve the pain. The shock should be treated by heat and fluids. Examination should be made for motion, sensation and circulation. This can usually be done without removing the dressing. If a fracture is suspected, x ray pictures are helpful. In the first six hours after injury, it is reasonably possible to cleanse the wound by mechanical means and to treat it as a clean wound. After this time the wound should be considered infected. As soon as possible the laceration should be cleaned and repaired under perfect aseptic surgical conditions. An anesthetic may be necessary. The open wound itself should be protected with sterile gauze, and the surrounding skin above and below the laceration carefully washed with soap and water.

Following this, the wound should be thoroughly lavaged with copious amounts of salt solution, and at the same time a thin wafer of injured skin edge and all devitalized material should be removed with sharp dissection. The bruised ends of the tendons and nerves may be refreshed. The lavage of salt solution should be continued with frequent changes of linen and instruments. The true cause of infection in wounds is bacteria, but most of the bacteria introduced into lacerations are not pathogenic or accustomed to living in the human being. Their ability to live and grow does not begin for several hours. By washing and débridement it is possible to render a wound relatively clean. It is amazing to note the ability of normal tissues to withstand bacteria if all devitalized material has been removed.

As noted before, a careful anatomical diagnosis is helpful. It is always discouraging on opening such a wound to find unsuspected lacerations of tendons, nerves and other structures. A constant flow of saline solution from an elevated irrigator should be continued until the débridement is finished. A smaller spray, continued during repair, keeps the tissues warm and moist.

Repair

Repair is best accomplished with simple silk sutures used to approximate tendons, nerves, fascia and skin. Bleeding is best controlled by pressure, only the large vessels being ligated. The tissues should be gently handled. Exposure is obtained with fine retractors or hooks. Grasping with forceps or hemostasis is to be avoided. The saline spray is continued until the skin is closed. If the

loss of skin is so severe that the wound cannot be closed, and especially if tendons, fascia or nerves are exposed, primary skin grafting is necessary. A razor or Thiersch graft should be cut and sewed snugly and firmly in place. This closes the entire wound. If this is done, infection, necrosis of tendons, loss of fascia and difficult contractures may be avoided.

Dressing

The dressing should be abundant, soft, cotton sponges. It should be reinforced by a thick three inch cushion of absorbent cotton extending well above and below, and held firmly in place by a cotton elastic bandage.

Splinting

Splinting gives rest and promotes healing and a splint made of wood, plaster of Paris or aluminum can be used. With no evidence of infection such wounds, carefully splinted, may be left for several days. If there are fractures, these must be aligned in proper position at the time of primary closure. The splint holds the bone in the reduced position. If skin grafts have been used they are best left alone until they have had an opportunity to grow in place.

TREATMENT OF WRINGER HANDS

There is a new and modern injury to the hand. A housewife, using her washing machine, has her hand drawn between the moving rubber rolls of the electric clothes wringer. Often it is drawn in above the wrist. After the compression is released the hand is removed. It is pale, it is only moderately sore and is sometimes anesthetic. X ray films reveal no fracture. Immediate treatment is all important. The hand should be elevated and an absorbent-cotton compression dressing should be applied, extending well above and below the injury. This must be held firmly in place with a cotton elastic bandage, and the hand maintained in the elevated position. If this is done edema of the subcutaneous tissues can be prevented and skin necrosis forestalled. The dressing must be removed, the hand inspected and pressure reapplied every four hours during the next two or three days. If the compression bandage is not applied, the hand will become swollen and edematous. The skin may become anesthetic, and necrosis of large skin areas may follow. Large rubber sponges, if available, are even better than the cotton pressure dressings. If one is alert and aggressive in this treatment it is possible to prevent swelling and later necrosis of the skin.

Sometimes the initial injury seems so slight that a physician is not consulted until several days later,

when a black necrotic area appears on the back of the hand

In children these injuries are even more severe, for the arm may be drawn in to the shoulder. The immediate appearance of the hand may not be bad, but the same active preventive measures should be instituted, with constant pressure and frequent inspection for forty-eight to seventy-four hours. Cases have been reported in which necrosis of the skin has been so extensive as to require skin grafting of the entire arm. The crucial and important time for action is during the first hour after the accident.

INJECTION TREATMENT OF HERNIAS

During the third century, Heliodorus described the operation for the radical cure of hernia. In 1893, Halsted wrote

The operation for the radical cure of hernia in the time of the Roman emperors was quite on a par with the operation as it is usually performed in our day. Four hundred years later the operation had ceased to exist. From that time to the introduction of antiseptic surgery, methods of all sorts, many of them cruel and some barbarous, have been in vogue. They may be classified as follows:

- 1 Pressure with or without the simultaneous application of irritating and so-called contracting remedies
- 2 Caustics and the actual cautery
- 3 Ligation of the sac, with or without cutting it off
- 4 Introduction of foreign bodies into the hernial sac
- 5 Healing in of a detached portion of skin, or of a portion of impacted skin into the abdominal ring
- 6 The injection of irritating fluids within or outside of the hernial sac
- 7 The subcutaneous suture.

Some of these methods are interesting as curiosities, and others because they are still practised. We are indebted to antiseptic surgery for reintroducing to us the operation of Heliodorus.

Recently the injection method has been resurrected and advocated in a voluminous literature. The claims made have been enthusiastic, and the inference has been that the results are uniformly satisfactory. Most of these reports, however, do not include end-result studies made several years after the termination of treatment. During the last decade the advocates of this method have narrowed their scope, until now practically all these writers agree that the only cases favorable for treatment are small, indirect inguinal hernias that can be reduced and kept reduced by a truss.

Still more recently the injection method has been subjected to critical review in several large clinics. In a report by Sowles and Shedden of the Massachusetts General Hospital, only half the cases pre-

sented for treatment were considered suitable. One hundred and nine cases were injected, with about twelve injections per patient. They state that the ideal patient is active, with good musculature, not obese and with an indirect inguinal hernia of small or moderate size. Under these conditions, the recurrence rate should be held at 25 per cent.

The Hospital for the Ruptured and Crippled in New York City sought to obtain first-hand information concerning the advantages, disadvantages and end results of the injection method of treatment. Fifty-eight patients were treated. Various solutions were used, but no one of them was shown to have any special value. End results in the 58 cases which could be traced showed that there were 47 known failures, of the 11 cases with possible cures, in 9 the patients were still wearing trusses.

In the meantime it has been shown that, considering all types of inguinal hernias in the hands of competent surgeons, the recurrence rate has been steadily decreasing, and at the present time is about 4 per cent.

In view of all this, it would seem that we are now passing through a cycle in the treatment of hernia, that the ideal treatment is still a carefully planned, well-done surgical operation and that injection treatment is distinctly limited in value and is not to be recommended.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 25481

PRESENTATION OF CASE

A sixteen year-old schoolgirl was admitted from an outside hospital to the Neurological Service because of convulsions of nine months duration.

The patient was delivered normally at full term. She subsequently developed normally until five years of age, eleven years before admission when she began having frequent daily, transitory "spells" lasting a few seconds and characterized by an upward rolling of the eyes and an inability to speak. These attacks continued unremittently for nine years until the age of fourteen or two years before entry, when they practically stopped. Catamenia began at that time and occurred regularly every month for one year with a profuse flow requiring six to eight pads a day for seven days. The menses ceased completely for the year prior to her admission, with the exception of a little spotting on two occasions. At the age of fifteen, about ten months before entry, throbbing occipital head aches, convulsions and a staggering gait appeared. She also developed a voracious appetite and gained 30 pounds in weight. The headaches began rather suddenly, lasted two or three days at a time, and stopped three months later to leave a residual "grinding sensation" in the back of her head and an almost constant ringing in both ears. With the head pain the patient would "arch her head way back" and toward the left. The convulsions occurred at monthly intervals and usually lasted about ten minutes. They began without warning and were characterized by a stiffening of the body with the mouth and head drawn to the left and clonic movements of the arms, especially the left, she would salivate, bite her tongue and become incontinent of urine. These episodes progressed in severity, with cyanosis during and marked stupor following the attacks. The staggering became an almost drunken gait for the two months before admission. There seemed to be a tendency to fall toward the left.

The patient had reached the first grade of high school. She seemed intellectually normal and did fairly well in her studies. She stopped going to school when her convulsive seizures began. During the two months before entry she became unusually nervous and inattentive. Her mother thought that her bearing and vision were at times

impaired. The patient withdrew from her friends, became less active and refused to do housework. She even stated that she was "no good anymore." Four days before admission the patient had four severe convulsions, she was seen by a physician who found "pressure behind the eyes" and advised immediate hospitalization. The patient had had German measles, measles, pertussis, chickenpox and mumps in early childhood but no other serious illnesses. She developed striae over both hips when she was twelve years old. Similar striae had been noted in one of the patient's four living sisters, most of whom were "stocky." One brother had had "convulsions" from the age of six months to four years, when they stopped. The mother was living and well although she had diabetes.

Physical examination revealed an inattentive, well-developed obese girl, who was lying in bed exhibiting moderate choreiform movements of the extremities face and tongue. Her cheeks were flushed, and there were reddish-blue striae over the hips. The heart was slightly enlarged to percussion. The aortic second sound was snapping and was louder than the pulmonic second sound. The blood pressure was 130 systolic, 90 diastolic. The lungs, abdomen and pelvis were normal. The extremities showed moderate but definite choreiform involuntary movements, most marked in the hands and arms. The neurological examination disclosed the following facts. She was inattentive, dull and unco-operative, but was oriented and lucid. Smell and taste were intact, the vision "adequate, but depressed" the visual fields could not be determined because of a lack of co-operation, she seemed incapable of fixing the eyes steadily on any object "due more to lack of concentration than to anything else," in the opinion of the examiner no gross defects were noted. There was bilateral edema of two to three diopters of the optic nerve heads. There were no hemorrhages or retinal tumors. The pupils were equal and regular, they reacted promptly to accommodation but failed to respond to light. The external ocular movements showed full lateral excursions, although the movements tended to be jerky. There was a limitation of upward gaze with diplopia on looking upward and poor convergence. There was no ptosis or nystagmus. No sensory loss over the face was noted and the corneal reflexes were obtained. There was a right facial asymmetry with weakness, and bilateral tinnitus with audiograms showing very slight conduction impairment and a tendency toward early nerve involvement. The tongue was in the midline, with normal movements there was no difficulty in swallowing. The gait was very unsteady. There was a tendency to fall to the left and backward. Rapid

and finer movements of the hands and arms appeared normal. There was a definite asynergia in the finger-to-nose test bilaterally. Hypotonia of the muscles was thought to be present. No definite athetoid movements were noticed, although odd positions of the arms and hands were frequently obtained. Muscular strength in the arms and legs was good, there was no atrophy. No sensory loss was made out in the grosser forms of sensation, although a questionable diminution in position sense was elicited in the arms and legs, especially on the left. Reflexes were equal but slightly depressed. The Babinski, Oppenheim and Chaddock signs were equivocal.

The temperature was 100°F, the pulse 110, and the respirations 20.

The urinary examination was negative, while that of the blood showed a red cell count of 5,000,000 and a white-cell count of 11,000 with 57 per cent polymorphonuclears. The blood Hinton test was negative. A sugar tolerance test read as follows: fasting, 95, thirty minutes, 191, one hour, 162, two hours, 154, and three hours, 91 mg per 100 cc. The ventricular tap fluid had a protein of 330 mg per 100 cc and was grossly bloody. The fluid was otherwise not examined. X-ray studies of the skull revealed a marked increase in the convolutional markings. The dorsum sellae was destroyed. The anterior clinoids were shortened. There was an area about 2 cm in diameter in the region of the pineal gland which contained multiple small flecks of calcification. Films of the hands were negative. The fingers were long. The distal epiphysis of the ulna was closed, the one in the radius almost closed. The development of the hands showed evidence of precocity. Films of the abdomen and chest were negative.

On the fifteenth hospital day the patient was operated on.

DIFFERENTIAL DIAGNOSIS

DR AUGUSTUS S. ROSE. In considering the diagnosis of this rather long case, there are several very striking features, both as to the nature of the lesion and its location. Our attention is attracted at once to the region of the midbrain. We have to deal with a girl of sixteen who had convulsions, headaches, visual disturbances, disturbances in hearing, metabolic disturbances, cessation of the menses and in addition a progressive difficulty in walking. On physical examination we find an obese girl with choked disks, pupils which were fixed to light but reacted well to accommodation, paralysis of upward gaze, which I believe is the key to the diagnosis, and in addition, signs of inco-ordinate asynergia in the finger-to-nose test, some decrease in muscular tone and

difficulty in walking. Furthermore, the x-ray films, the choked disks, the history of headaches and the destruction of the dorsum sellae are all confirmatory of increased intracranial pressure. The flecks of calcium in the region of the pineal gland cannot be considered normal, and in my opinion in themselves probably warrant the assumption of a tumor. If, then, this reasoning, that we have to deal with a tumor in the region of the pineal gland causing blocking of the aqueduct with an internal hydrocephalus, is correct, how are we to explain the symptoms, and further, where does the tumor originate? We have to consider the following: (1) the pineal gland or immediate vicinity, (2) the hypothalamus or region of the third ventricle, (3) the midline cerebellar region, high in the vermis, and (4) a primary tumor in the midbrain itself.

To consider these in reverse order, from my brief experience I have never seen a case of primary tumor of the midbrain, and in a hurried search last night in various textbooks and one or two journals, I was unable to find a single case of primary tumor in the midbrain that could not be interpreted as pinealoma. They must exist but probably are extremely rare. Furthermore, if the tumor originated in the midbrain we should expect more long-tract signs, for example hemiparesis or more definite evidence of unilateral sensory involvement. Furthermore, we should expect the third or fourth cranial nerve to be more definitely involved. As for the midline cerebellum, discussion is a little more difficult. Cerebellar tumors are prone to occur in children, particularly medulloblastomas, are likely to be located in the midline and notoriously have poor localizing signs, block the aqueduct, cause marked increase in intracranial pressure, with internal hydrocephalus, and cause secondary pressure changes such as are found in the x-ray film of this case. Furthermore, this patient had signs which we must interpret as being true cerebellar signs. She had loss in muscle tone, asynergia, staggering gait, without paralysis, and decreased reflexes. But the assumption of tumor in the midline cerebellum leaves unexplained the x-ray findings of flecks of calcium above the tentorium and in addition, it is my belief that paralysis of upward gaze and disturbance in the light reflex of the pupil do not occur in subtentorial tumors, nor do they occur secondary to increased intracranial pressure. Furthermore, paralysis of upward gaze which is a supranuclear difficulty has been definitely located in the pretectal region just in front of the superior colliculus. In the same region, just beneath the pineal gland, there are fibers which transmit the light reflex. On the basis of

these two findings interpreted in the light of these physiological facts plus the x-ray I rule out midline cerebellar tumor.

Could it arise from the hypothalamus or the region of the third ventricle? Using the same line of reasoning we should expect symptoms of metabolic disturbances and other difficulties to arise early and be more prominent, and furthermore, you would not expect these same findings that I have just mentioned. We are left, then, with a tumor of the pineal gland or of the region immediately near the pineal gland as the best explanation.

Does a pinealoma explain the whole group of symptoms? I think it does. Dr. Mallory is prone to give us something that may trip us up once in a while, but in looking over the literature and the description of pinealoma, this case might easily be inserted into a textbook as a classical case with the exception of two groups of symptoms. A pinealoma is a soft tumor which infiltrates only a relatively small area of the midbrain. It usually grows upward and, by virtue of the position underneath the corpus callosum and in between the cerebral hemispheres just above the tentorium cerebelli, it grows forward into the third ventricle. Symptoms of disturbance of hypothalamic function result from direct extension of the tumor or by pressure. Furthermore, this patient had disturbances in hearing or in auditory function and an ear consultant suggested the possibility of early nerve deafness. This can be explained easily on the interruption and irritation of fibers of the lateral lemnisci or the medial geniculate bodies which are in the same vicinity.

Thus far I have purposely left out discussion of the convulsions. Convulsions of this sort can occur in so-called cerebellar fits. These tend to simulate decerebrate rigidity. They go out of the way to tell us that there was extension or retraction of the head in this case and very marked cyanosis although there were some clonic movements of the extremities. The convulsions can be explained either by generalized increased intracranial pressure or by a functional decerebration at the level of the midbrain. Convulsions due to the latter cause can occur in cases with pinealomas, third ventricle tumors or subtentorial tumors.

There are two other groups of symptoms in this case, however, which I think are somewhat more difficult to explain. First, the spells which were of eleven years duration and ceased about the time that we are given to understand the present illness began. If there was a pinealoma present I am not prepared to say it was the

cause of these spells. It is of great interest, however, to note that these spells which lasted for a few seconds were characterized by upward rotation of the eyes and an inability to speak. Before 1900, Sherrington demonstrated in dogs and monkeys experimentally that stimulation of the region of the superior colliculus produced deviation of the eyes, laterally or upward. Stimulation of the posterior colliculus produced phonation. Let us put that in for what it is worth. No cases of pineal tumor that I have reviewed had symptoms of choreiform movements. Frankly, I cannot explain them. However, the subthalamic nuclei or the corpora luyssi, which are small nuclear masses situated slightly anterior to the region concerned, are known to be associated with involuntary movements. If one of them is involved by hemorrhage or thrombosis, marked unilateral choreiform movements occur. Possibly the tumor has encroached upon this region.

My diagnosis, therefore, is pinealoma with internal hydrocephalus. I should like to emphasize that the most important sign in this case, including the x-ray findings, is the paralysis of upward gaze.

DR. RICHARD SCHATZKI. I cannot add very much to the description given in the abstract. The x-ray picture is that of increased intracranial pressure with marked thinning of the skull in the region of the convolutional markings. The sella is enlarged and the dorsum sella is destroyed which can be due either to a local process or to increase in the intracranial pressure. The relative uninvolvedness of the anterior clinoids is in favor of a local process, pressing on the posterior clinoids, although I do not believe that this holds true in all cases. Very often one cannot make a differential diagnosis of destruction due to local disease and that due to generalized intracranial pressure. The most important findings are these three specks of calcification which you may not see from a distance, and which I cannot see in the anteroposterior or posteroanterior view, but which apparently, judging from the report were seen stereoscopically to lie fairly well in the midline. You would expect this to be the region of the lesion, with possibly pressure on the aqueduct producing increase in intracranial pressure.

DR. JAMES B. AYER. I wish to congratulate Dr. Rose on his excellent analysis of the case. I was particularly interested in his ideas concerning the mechanism of the convulsions. Perhaps his explanation of pressure as a cause of decerebrate rigidity is correct. I also wish to emphasize the importance of the eye finding in particular of

course the paralysis of upward gaze, as indicating a lesion of the upper midbrain and as a sign very characteristic of pineal tumor. In this connection I might cite a case studied by us within the past year. This man appeared to me to have a frontal lobe abscess. I tried to explain his weakness of upward gaze on the basis of a supranuclear lesion. Dr. Kubik interpreted the case correctly as one of midbrain involvement, and a pineal tumor was found at autopsy. Paralysis of upward gaze appears to be one of the most dependable signs in neurology.

One thing Dr. Rose did not stress was the endocrine picture. This aspect of the case was discussed at a recent neurological staff meeting, and all who were present agreed it was very unusual to find endocrine disturbance caused by pineal tumor, particularly in the female. Reference was made to an article by Horrax and Bailey* which bore out this point. In the twelve cases studied by them were only two girls, who were ten and fifteen years of age. The younger showed no evidence of pubertas praecox. The older had reached maturity at thirteen years. Furthermore these authors cite no examples from the literature of early maturity in girls in whom pineal tumor is present.

DR. TRACY B. MALLORY: In several of Dr. Horrax's boys there was definite precocious puberty. As I remember he observed a sharp difference in the two sexes, frequent endocrinopathy in the male and rare in the female. Even in the boys, however, it was not always present.

DR. J. H. MEANS: The endocrine manifestations associated with pineal lesions might well be due to encroachment on the pituitary. Would that be possible?

DR. AYER: I suppose it is very likely.

DR. MALLORY: Increased intracranial pressure alone will produce considerable hypertrophy of the adrenal glands, and many of the other endocrine glands, I suspect, would be secondarily implicated.

DR. HENRY R. VIETS: One significant point is in regard to the Argyll-Robertson pupils. In this case they are not due to neurosyphilis, but to a lesion of the quadrigeminal plate. The pupils are typical of the Argyll-Robertson type in that they do not respond to light but do to accommodation. One misses, however, the myosis and the irregularity of the pupil so suggestive of neurosyphilis.

CLINICAL DIAGNOSIS

Pinealoma

*Horrax, G. and Bailey, P. Tumors of the pineal body. Arch. Neurol. & Psychiat. 13: 423-470, 1925.

DR. ROSE'S DIAGNOSES

Pinealoma
Internal hydrocephalus

ANATOMICAL DIAGNOSES

Primary tumor of pineal, ? medulloblastoma

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient was operated on by Dr. Hodgson who after laying back a frontal bone flap exposed the third ventricle which proved to be markedly hydrocephalic. A ventriculotomy was performed without attempting to reach the tumor. Convalescence was uneventful and on the seventh day x-ray therapy was begun and seemed to be well tolerated until the sixteenth postoperative day, when she suddenly became cyanotic and died within a few minutes.

The autopsy was unfortunately limited to examination through the craniotomy wound so we can supply no data as to the condition of the various endocrine glands. No explanation was found within the head for the sudden demise, but Dr. Kubik can tell us more about the tumor.

DR. CHARLES S. KUBIK: Although autopsy was restricted to examination through the craniotomy wound a satisfactory view could be obtained. There was a discrete, ovoid tumor, measuring 4.5 by 3.5 by 2.5 cm. in the midline in the pineal region, just where Dr. Rose thought it would be. Although it did not seem to involve any of the adjacent tissues one cannot be altogether certain without a microscopic examination that there was no invasion of the tegmen of the midbrain. Despite its apparent origin in the pineal gland, histologically the tumor does not resemble pinealoma or pineoblastoma. An outstanding feature was the presence of columnar cells arranged radially around blood vessels and suggestive of ependymoma. Of course Cushing used to say that so long as there was a good deal of uncertainty as to the classification of tumors in this locality it was best to call them pinealomas anyway, that is, to be guided by position rather than histologic appearance.

Nothing that might have accounted for the seizures was found in the cerebral hemispheres.

DR. ROSE: Would you make an estimation of how long the patient had had the tumor?

DR. KUBIK: I could not, but it was probably a long time. I have not found calcium in any of the sections.

DR. SCHATZKI: Did you take x-ray films of the specimen?

DR. KUBIK: No.

CASE 25482

PRESENTATION OF CASE

A sixty five year-old English born carpenter was admitted complaining of a gastric ulcer."

About twenty years before admission, without prodromal symptoms or pain the patient had suddenly vomited a large amount of "black blood," fainted and later passed black stools. He was treated by an outside physician with rest, a Sippy diet, liver and iron. Nearly every year following this episode the patient had at some time, noticed tarry stools and weakness, but he had had no vomiting, he was treated in the same way but became careless of the regimen between the spells when he felt well. One year before entry he had twice noted the passage of tarry stools for periods of two weeks each. For six months before admission the patient felt a lump in his throat on swallowing he began vomiting small amounts of recently ingested food though this occurred only about once a week. He developed heartburn after eating which was only partly relieved by milk and soda and which sometimes persisted all night. He had lost 15 pounds in weight, but stated that he had been eating less.

The patient was first examined in the Diagnostic Clinic. The physical examination there showed slight tenderness near the umbilicus but no palpable masses. A gastrointestinal series performed five days before admission showed no evidence of disease in the esophagus. The gastric mucosa was smooth and pliable throughout showing no filling defects. In the cardiac portion of the stomach there was an area suggesting a filling defect which projected into the lumen this was not constant. There was definite tenderness over the duodenal cap, which showed a clover leaf deformity with a 4 mm ulcer crater the rugae converged toward the crater. Two days after the x-ray studies, or three days before admission the patient again began having tarry stools. These continued until admission. He also began raising small amounts of blood by retching less than a half teacupful in all. He complained of great weakness and of a very uncomfortable substernal "nauseated feeling." Because of these symptoms he was referred to the hospital for further studies and treatment.

The physical examination revealed a very pale, slender man lying in bed in no acute distress. The teeth were carious the peripheral arteries somewhat sclerotic. The pulse was slow and of good volume, and the blood pressure was 110 systolic, 60 diastolic. The heart and lungs were normal. Superficial palpation of the abdomen was nega-

tive except for the presence of slight tenderness immediately to the left of the umbilicus. At a more thorough examination later, firm masses, probably scybala, were felt in the left upper quadrant. By rectum two hard nodules were palpated in the rectovesical pouch.

The temperature was 98°F., the pulse 82, and the respirations 18.

Examination of the blood showed a red-cell count of 2,000,000 with 32 per cent hemoglobin (Sahli), and a white-cell count of 8200 with 88 per cent polymorphonuclears. The urine was negative, and the stools were brown and formed, with a + guaiac test, the vomitus gave a ++++ guaiac test. The serum protein was 5.6 gm per 100 cc., and the carbon-dioxide combining power, nonprotein nitrogen and chlorides normal. Roentgenograms of the abdomen taken about twelve days after the gastrointestinal series in the Out Patient Department showed that practically all the barium given then lay in the colon. Above this there were several loops of small bowel filled with gas. No definite free air was visualized in the peritoneal cavity, although the diaphragms on the anteroposterior view were not visualized on the film. The patient was given eight 500-cc. blood transfusions in nine days and his blood count rose to 3,200,000 with a hemoglobin of 60 per cent. On the second and third hospital days the temperature rose to 101.2°F., on the third day to 104, and subsequently fell to 99 for the ensuing days until he was operated on on the ninth day after admission.

DIFFERENTIAL DIAGNOSIS

DR. ALLEN G. BRAILEY "He was treated by an outside physician with rest, a Sippy diet, liver and iron. Twenty years ago the specific benefits of liver in anemia were not known so I do not know why liver was given."

Two days after the x-ray studies, or three days before admission the patient again began having tarry stools." This was possibly the result of having been examined but perhaps only a coincidence.

I should like to look at the x-rays.

DR. AUBREY O. HAMPTON "There is certainly a duodenal ulcer and it appears in some of the films that there is an active ulcer crater. The thing that worries me more than the ulcer is the questionable defect in the cardiac region of the stomach. I wish I could make a fluoroscopic examination."

DR. BRAILEY "What about the dilated loops of small intestine which are mentioned?"

DR. HAMPTON "These films of the abdomen are of such poor quality that the only certain thing

is that there is barium in the colon from the examination done twelve days before. The colon is not very large, but in this area it looks as though there is spasm in the descending portion. I should suspect obstruction of the sigmoid in addition to the lesions in the duodenum and in the fundus of the stomach.

DR. BRAILEY: There does not seem to be any question about his having had a duodenal ulcer. The history does not have much to say about the pain after meals which is characteristic of ulcer, but we know peptic ulcers may develop and may repeatedly bleed without much pain. He had repeated hemorrhages, as a result of which he vomited blood, so one would suspect at least one source of bleeding not far below the pylorus. Then, of course, there is the confirming x-ray information in regard to duodenal ulcer. The question is raised as to whether this ulcer perforated. I do not see that we can be certain of that. It is the type of ulcer that very likely penetrated deeply and may have perforated. There was certainly no evidence of perforation on physical examination or from the symptomatology other than the fact that he developed fever on the second and third days. The fever occurred in the course of eight transfusions, and he may have had a febrile reaction to one of these. If his fever was due to perforation it must certainly have resulted in a very localized peritonitis, because nothing is said about the pain or rigidity of the abdominal wall that is characteristic of generalized peritonitis.

How much of a case can one build up in favor of cancer? There was a loss of 15 pounds in weight. The history does not state over what period of time. The intestinal tract was filled with old blood for long periods, he had been nauseated and of course he had anorexia so I cannot see that this weight loss suggests cancer. He ought to have lost weight in any case. Then we have the x-rays done in the Diagnostic Clinic. It would be comforting to know more about this defect in the cardiac portion of the stomach, which apparently is something, but nobody seems to know quite what. We shall have to leave it there for the moment.

What seems the most important point in the entire case is that on rectal examination two hard nodules were palpated. If the examiner felt two hard nodules it must have been a very definite impression, and his observation can be trusted. Nodules in that location are almost invariably due to cancer, I believe. I have tried to think of other things which might readily be felt in that location, such as filled diverticula of the sigmoid or possibly mesenteric nodes, but I am sure that even if they were described as hard nodules they would

be fairly freely movable unless adherent as a result of inflammation. If these nodules were metastases, where was the primary cancer? Cancer of the duodenum is so excessively rare that a diagnosis should seldom be made. These nodules may have been due to lymphoma, or they may have been metastases from a carcinoma of the sigmoid, or even of the small intestine, of which we have little other evidence. But the x-ray examination gave what I believe was a helpful hint when it suggested a filling defect at the cardiac end of the stomach. I think that this man had duodenal ulcer which was the source of bleeding, but that he also had carcinoma of the stomach with peritoneal metastases.

DR. TRACY B. MALLORY: I should like to ask Dr. Brailey if he makes anything of the substernal discomfort.

DR. BRAILEY: Presumably it is important, since I have been asked. The heartburn which he complained of simply means esophageal spasm which characteristically occurs in any case of duodenal ulcer, and I passed that by simply as discomfort which was not unlike heartburn. I was willing to exclude disease of the esophagus as such because of the x-ray report.

DR. MALLORY: You did attribute it to presumable spasm of the cardia?

DR. BRAILEY: Yes.

DR. MALLORY: Are there any other suggestions?

DR. HAMPTON: I think that the mucosa is abnormal both in the lower end of the esophagus and in the fundus of the stomach.

CLINICAL DIAGNOSES

Hemorrhage from peptic ulcer
Pulmonary edema
Bronchopneumonia?

DR. BRAILEY'S DIAGNOSES

Bleeding duodenal ulcer
Carcinoma of stomach with peritoneal metastases

ANATOMICAL DIAGNOSES

Carcinoma of the stomach, with extension to the esophagus and with metastases to the liver, left kidney and mesenteric lymph nodes
Operative wound jejunostomy
Recent leakage around the jejunostomy tube
Intestinal obstruction, subacute, small and large bowel
Duodenal ulcer, healed
Pulmonary edema
Vascular nephritis

PATHOLOGICAL DISCUSSION

DR. MALLORY Dr Brailey has seized on the essential feature of this case, namely, that the readily demonstrable duodenal ulcer was an inadequate explanation of the clinical picture and that some other lesion must have been present in the gastrointestinal tract. The ordinary gastroenteroscopy series is by no means infallible. The cardiac antrum is always difficult to visualize and lesions of the small bowel frequently escape attention unless the radiologist's suspicion is aroused and the patient is repeatedly examined at rather short intervals. It is too bad that this patient was not gastroscopied, as almost certainly the lesion would have been picked up by that method. There was a large infiltrating carcinoma of the cardiac portion of the stomach which extended up into the esophagus. It involved nearly 6 cm of the lesser curvature and a larger portion of the greater curvature. Well up in the cardia was a large crater 3 cm in diameter with a ragged necrotic base. This I am sure was the source of the hemorrhages. We had a little difficulty in finding the duodenal ulcer. It was there but was inactive so far as we could make out.

DR. HAMPTON It should not have been active if he had carcinoma of the stomach. What did he have wrong with the colon?

DR. MALLORY There were some dense fibrous adhesions about the hepatic flexure which caused an acute angulation and the cecum was considerably distended. There were relatively few metastases. Even the liver showed only one, but there were definite microscopic metastases found in the bone marrow.

DR. BRAILEY Why did the surgical service operate on him?

DR. FIORINDO A. SIMEONE This man was steadily going downhill and was vomiting a great deal. The operation performed was a jejunostomy in the hope that he might improve sufficiently to permit further study and later perhaps exploratory operation. He lived only seven days after his jejunostomy.

DR. MALLORY This is the sort of case which occasionally is cited as evidence that a chronic benign ulcer turns into a carcinoma but in this case we have the evidence that the ulcer was duodenal whereas the cancer was in the upper end of the stomach, and there is no possible connection.

The New England Journal of Medicine

Formerly the

Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

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THE NEW HAMPSHIRE MEDICAL SOCIETY
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SUBSCRIPTION TERMS: \$6.00 per year in advance postage paid for the United States; Canada, \$7.04 per year; \$8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

WILL PROPRIETARY MEDICAL SCHOOLS BE APPROVED?

THE circular letter from the Approving Authority for colleges, universities and medical schools, which appears on another page of this issue of the *Journal* and which has been sent to all medical schools and state boards of registration in medicine, as well as given to the press, brings again to the attention of the public the fact that the attitude of Massachusetts toward medical education has changed recently in an important respect. Accompanying the letter are copies of the statute creating the Authority and of the "Requirements for Approval of Colleges, Universities and Medical Schools," first published, in accordance with the statute, in the autumn of 1936. It is timely to discuss some of the provisions of the law and of the rulings by the Authority.

The Authority seems to have no initiative in the matter of approval, and the basic assumption is that all schools are disqualified until approved. Stated another way, no graduate of any medical school, unless he is exempted by the statute, may be admitted to examination by the Board of Registration in Medicine until the school has asked for and has received approval.

The rulings of the Authority on qualifications required for approval of a college or university show that the education required is to be approximately at the level of a low general average. No individual excellence is required, and the qualifications represent a minimum considerably below what is offered by most students seeking admission to medical schools today. An institution whose students merely meet this minimum will be generally considered to be, and probably will be, a low-grade school. Although colleges and universities must be approved as of this fall for students admitted to medical schools in the fall of 1941, no public statement in regard to this point has been made by the Authority.

The requirements for approval of a medical school are more specific and more interesting, and frequently contain the word "adequate." The preclinical courses, the laboratories, the equipment, the clinical material and the professors must be "adequate." Knowledge of what this means in medical education is widespread. By contrast, there was a medical school which described in its catalogue the obstetric material for teaching as "ample." However, the official returns for the county in which the school was situated and for the four adjacent counties indicated that over a period of five years the number of births had been such as to give an average of less than one birth per student per year, and a considerable number of these were not available for teaching purposes. The checking of the statements in some medical school catalogue against the facts is a time-consuming procedure but often very illuminating.

In spite of the elasticity of the word "adequate," very properly used in educational matters but almost horrent to those persons who stress the value of

forms and other externals, the net gain seems to be that the requirements may result in a very pedestrian minimum instead of a reasonably high general average. Massachusetts may continue to have some of the poorest medical schools in the United States but these may not be quite so low in grade as they are at present. This is one of the possible weaknesses of attempting improvement by legislation: statutory standards properly attain only a minimum level.

Evaluation of medical schools is not a procedure which the Approving Authority has had to create. Rather searching questionnaires were employed in the recently completed survey of medical schools in the United States and Canada, these had to be filled out and returned and were studied before the inspectors visited the schools. Perhaps the Authority may be able to take advantage of the experience that was gained in this study.

There has been some loose talk about the compulsory closure of medical schools in connection both with the activities of the American Medical Association and with those of the Approving Authority. Neither body has the power to close any medical school. But the strength of the Approving Authority lies apparently in the very procedure which seems at first glance to have been designed merely to protect the school, namely the court review. If a school appeals from the decision of the Authority, the court procedure and the authorization needed by the Authority to make public the basis for its decision. It is this finding of fact, made public, which the proprietary schools have most feared and have always been able to avoid.

The test of the "adequacy" of a medical school as of any educational institution, is, in the language of the market place, Does it deliver the goods? This pragmatic test may be very difficult to apply in fact. Who is authorized to make a study of the practice of each physician to see if he is really fulfilling his obligations? Would such study be justified? But a comparative test can and has been made. If only 5 per cent of the graduates of one medical school pass the state-board examina-

tions each year, and only 5 per cent of those of another school fail, would the public need any further evidence that the first school should be prevented from giving its poor substitute for medical education, no matter how low its tuition fee? And what if its tuition fee be the same or even higher than that of the second school? In the wool trade there are standards for shoddy, why not in education? If the public can be informed of the facts, they will demand the change. The Approving Authority can apparently perform its function best by a careful accumulation of facts for use in court. It is because proprietary medical schools have been able to suppress the facts that they have had their day.

NOBEL PRIZE WINNERS FOR 1938-39

The Nobel prize winners for 1938-39 have been announced. For 1938, the prize goes to Professor Corneille Heymans, of Ghent, Belgium, professor of general therapeutics at the University of Ghent. Professor Heymans's work has been on circulation and respiration. He was an early contributor to our knowledge of the carotid sinus and has written extensively on vascular tone, vasomotor reflexes and experimental arterial hypertension.

The prize for 1939 has been given to Dr Gerhart Domagk, of Wuppertal, Germany, for his work on the therapeutic effects of the derivatives of azo dyes. These substances had been used in the textile industry for many years. In 1913 Eisenberg studied their effects on bacteria and introduced chrysoidin as a chemotherapeutic agent. Although this drug gave excellent bactericidal results in vitro, the effects were not so good in experimental animals. In 1932, another azo compound was synthesized, a derivative of chrysoidin. It was this preparation that Domagk worked with and found strongly protective when given intravenously to mice infected with streptococci. A salt of the same drug was then introduced under the trade name of Prontosil. It was soon pointed out, however, that a slightly different substance, *p*-aminobenzene-sulfonamide, was the active agent and

this has been used widely ever since that date under the name of sulfanilamide

The important writings by Heymans and Domagk are on exhibit at the Boston Medical Library. In connection with the Heymans exhibit, it will be remembered that he gave the Dunham Lectures at the Harvard Medical School in November, 1937, and that his lectures were published in the *Journal* in August, 1938

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330 Dartmouth Street
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TOXIC SEPARATION OF THE PLACENTA, WITH FATAL GAS-BACILLUS INFECTION

Mrs. E. D., a thirty-eight-year-old para V, when thirty-six weeks pregnant, was readmitted to the hospital August 27, 1939, with a story of having had blurring and blackness of vision two hours before entry and having felt that she was going to faint but not actually losing consciousness. For two days there had been no fetal motion. A local doctor was called because of the above symptoms plus the fact that she had had mild abdominal pain and had passed one teaspoonful of bright-red blood per vaginam. He performed a vaginal examination, then sent her to the hospital.

The family history was not recorded. The patient had been well in the past except for recurring attacks of arthritis. At the age of five she had had scarlet fever. In 1928 a dilatation and curettage was performed for an incomplete early abortion. Three other pregnancies had terminated at term without complications. The menstrual periods had been normal and regular except for interruptions during pregnancies. The last menstrual period had begun December 26, 1938, making the expected date of confinement October 1.

The prenatal course was complicated by albuminuria and hypertension. She had been in the hospital from August 15 to 21 for study. At this time she was asymptomatic. Her blood pressure was 166 systolic, 92 diastolic, on entry but was 140

systolic at discharge. She was referred to the toxemia clinic.

On admission to the hospital on August 27 there was no edema except for slight puffiness about the face. The skin was cool to touch. She was perspiring and apprehensive. The pupils reacted to light and accommodation. The chest showed normal expansion, and the lungs were clear. The heart was not enlarged, and there were no murmurs. The pulse was 84, and the blood pressure 120 systolic, 90 diastolic. The abdomen was obese. There was generalized tenderness over the uterus. The fundus was three fingerbreadths below the xiphoid process. The baby was presenting by the vertex in an ROA position, and the fetal heart was not heard. The uterus was contracting about every three minutes and did not completely relax between contractions. No urine was obtained by catheterization. A diagnosis of toxic separation of the placenta was made. She was immediately given 1000 cc. of 5 per cent glucose solution intravenously. Donors were obtained for transfusion.

Two hours following entry the patient was examined under nitrous oxide and oxygen anesthesia. The cervix was high up under the symphysis and was 2.5 cm. in length. The external os admitted a fingertip, and the internal os was completely closed. The presenting part was high and movable. Attempts were gently made to insert the index finger through the internal os in order to reach the membranes, but this could not be accomplished. Mechanical dilatation was not performed. A cervical pack, previously dipped in 3.5 per cent iodine solution, was inserted into the external os. The vagina was then tightly packed with sterile gauze. There was very little bleeding during this procedure. The patient was then allowed to come out of anesthesia and a Spanish windlass binder was applied to the abdomen. Following this she had contractions at two-minute intervals lasting approximately forty-five seconds. The pulse was 120, the blood pressure was 158 systolic, 110 diastolic. The patient complained of constant pain in the back, as well as pain with contractions.

At 8 p.m., six hours after entry, the patient passed 50 cc. of dark-colored urine through an indwelling catheter, and this became solid when boiled on examination for albumin. Her blood pressure had risen to 170 systolic, so she was given 20 cc. of a 10 per cent magnesium sulfate solution intravenously. She was receiving Infundin in 1-minim doses because the uterine contractions were weaker. Because of extreme restlessness the patient was given $\frac{1}{4}$ gr. of morphine subcutaneously and 20 gr. of chloral hydrate by rectum.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

Because of lack of progress and inability to rupture the membranes on the first examination, she was re-examined under aseptic precautions at 11 p.m. on the evening of admission at which time the cervix admitted one finger. The membranes were ruptured. About 150 cc. of light greenish fluid was obtained. There was no bleeding. The abdominal binder was re-applied and Infundin stimulation was continued with 1 minim doses. The temperature twelve hours after admission was 97.6°F.

At 8 a.m. on August 28, eighteen hours after entry, her general condition was somewhat improved so far as color and responsiveness were concerned. Contractions were of very mild nature in spite of Infundin in 3-minim doses at hourly intervals. The temperature was 99.4°F., the pulse 100, and the blood pressure 174 systolic, 124 diastolic. Three hours later the systolic pressure was 210, so she was given a second dose of intravenous magnesium sulfate, 20 cc. of a 10 per cent solution. Urine in the drainage bottle at that time measured 150 cc.

At 1.30 p.m., twenty-one hours after admission a third vaginal examination was performed under ether anesthesia, with the hope of performing a Braxton Hicks version. The cervix was dilated only to admit one and a half fingers. It was impossible to bring down a foot. The lower segment and cervix were again packed with gauze. She was again started on Infundin stimulation, beginning with 2 minims and working up to 3 minims every forty minutes for four hours. She was given 200 cc. of a 25 per cent glucose solution intravenously at 3 p.m. At 4 p.m. her temperature was 100°F., the pulse 120, the respirations 38, and the blood pressure 168 systolic.

At 8.30 p.m. her pulse suddenly rose to 160 and the blood pressure dropped to 75 systolic. She presented a picture of sudden and extreme collapse. A glucose infusion was immediately started and was followed by 600 cc. of citrated blood. In spite of transfusion she expired at 9.32 p.m., about an hour after her sudden vascular collapse. A moderate amount of crepitation was felt over the suprapubic fatty tissue shortly before the patient expired.

A postmortem examination revealed premature separation of a normally implanted placenta. The cause of death, however, was an overwhelming generalized infection due to *Clostridium welchii*.

Comment. Gas-bacillus infection during pregnancy is fortunately very uncommon. It is quite likely that at the time of one of the vaginal examinations the organism was introduced.

This case presented a very serious toxemia as-

sociated with separated placenta when she entered the hospital at the second admission. The cervix undoubtedly was unfavorable to any form of induction. It is barely possible that if the cervix had been instrumentally dilated sufficiently when the first examination was made to allow the rupture of the membranes with or without the insertion of a bag that labor would have resulted much more favorably. The use of divided doses of pituitary extract for the purpose of stimulating labor, even in association with irritating stimuli such as those caused by cervical packing, fortunately does no harm, but it frequently does no good. In retrospect it is possible that cesarean section even in the face of a dead baby represents a mode of treatment which in this case at least might have been more successful than the more conservative method of cervical induction. The diagnosis of gas-bacillus infection was not suspected until the patient was seen on the autopsy table. At that time the skin of the face, arms, abdomen and legs was very much distended, crepitation was felt everywhere.

It is with a certain amount of reticence that this case is published in toto because of the possible influence it may have on the indiscriminate use of pituitary extract. For the purpose of inducing labor small amounts of the drug can be given without having any effect, a fact which means the causing of no harm, but its safe, indiscriminate use during labor cannot be deduced from this fact. During labor it must be used with the greatest amount of discretion. It is by far safer never to use it until full dilatation is present, being sure that there is no cephalopelvic disproportion.

REPORT OF THE COMMITTEE ON INDUSTRIAL HEALTH

THE PHYSICAL EXAMINATION IN INDUSTRY

The physical examination in industry is the foundation on which a good industrial medical service is built. Its object is to evaluate the physical status of employees and to observe that status by subsequent periodical re-examinations. Examinations thus are divided into pre-employment and periodic examinations.

Two things should be accomplished as a result of the pre-employment examination, first an appraisal of the physical condition of the prospective worker and of his ability to assume the work to which he is to be assigned, second, an effort on the part of the examining physician to prevent a man with contagious disease from working in contact with others or doing work which, because

of his physical condition, would be dangerous to the man himself or to others. The object of the examination is not to reject an applicant, rather it is an effort so to place a worker that he will be protected from contagion or from injury caused by his own or another's physical defects.

The periodic examination is made in order to check at regular intervals the condition of the worker, to discuss with him any defects or abnormalities discovered and to advise him as to their care. It may be an annual or a biennial event depending on the general condition of the individual and the health hazards to which he may be exposed at his work. In cases where the worker is exposed to any industrial hazard of a serious nature, the examination is made more frequently, with special emphasis on the signs and symptoms of early injury to health.

The method of conducting a physical examination in industry is becoming more or less standardized. It must be remembered, however, that the objects sought are not those of the life-insurance examination. The life-insurance examiner is particularly interested in the applicant's basic condition. His problem is to estimate the probable longevity of his patient. The industrial physician, on the other hand, is primarily interested in the probable working capacity of the individual, and he therefore appraises with great care certain abilities and functions which are comparatively unimportant to the life-insurance examiner. It is particularly important that the general practitioner who is called in by a neighboring factory to make examination of its workers should bear this distinction in mind.

The industrial physical examination is made in privacy in a suitably equipped room. The worker, if young, is examined completely stripped. Older workers are examined stripped to the waist at the start, later the trousers and underclothes are removed. The following routine of examination is suggested as a basis to which additions may be made if necessary.

Height
Weight
General appearance
Skin
Eyes (condition, reflexes, abnormalities), including vision in twenties and Snellen charts (each eye separately)
Ears (discharge), including hearing test with watch (Standard Yankee) at varying distances (each ear separately)
Nose (obstructions, deviation of septum and so forth)
Throat (condition of tonsils, pharynx and so forth)
Teeth (condition of gums, teeth needing extraction and so forth)
Neck (enlarged glands and so forth)
Chest contour (flat, emphysematous and so forth)

Chest expansion (inspiration and expiration measurement at nipple line), ability to hold breath 30 seconds
Heart.
Lungs
Pulse.
Blood pressure
Arteriosclerosis (present or absent)
Abdomen
Inguinal region (if hernia found, the type and degree)
Upper extremities (loss of fingers and so forth)
Lower extremities (varicose veins, ulcers, condition of feet and so forth)
Joints (restriction of motion, abnormalities of any kind)
Rectum (digital examination)
Genitourinary system, including prostate.
Spine, including all motions
Reflexes (knee jerks especially)
Urinalysis (if albumin present, microscopic examination)
Blood (if indicated)
X ray of chest (when indicated and in cases which will be exposed to a dust hazard)

The following defects have been found to be of particular importance

Markedly defective vision uncompensated by glasses, blindness of one eye.
Marked deafness of both ears
Hyperthyroidism
Myocarditis
Pulmonary tuberculosis, pleurisy with effusion
Emphysema and chronic bronchitis, asthma, fibrosis of lung
Glycosuria
Chronic appendicitis
Hypertension
Chronic nephritis, with acute exacerbation
Gonorrhea or syphilis, especially in active stage.
Chronic arthritis, especially of the spine
Ankylosis of important joints
Severe varicose veins, especially with edema of leg
Chronic foot strain, deformities of foot or toes
Hernias of all types
Hypertrophy or infection of prostate.
Diseases of nervous system.
Dental conditions suggesting foci of infection

The following parts of the worker's body should be given special attention: the eyes, the joints, the nervous system, the inguinal region, the condition of the extremities, the feet and the lungs.

The examining physician must not reject an applicant unless there is a very good reason. Where there is question, the worker should be passed but called back after a reasonable period and re-examined. It is good practice in these questionable cases for the doctor to visit the employee at his work in order to see just what he is doing and whether he appears able to do it without harm.

There are frequent cases where the applicant can work with greater safety and efficiency elsewhere than at the job for which he has been hired.

The doctor in these cases should discuss the matter with the employment manager or foreman and see if the worker cannot be employed at the more suitable type of work. A man is hired because he appears to the employment officer to have good qualifications for service in the company. The doctor must always remember this and see that in questionable cases every effort is made to render this service harmless to the man and of value to the company.

The pre-employment examination offers a splendid opportunity for the doctor to discuss with the applicant any abnormalities found during the examination and to tell him how such conditions may be rectified.

Those employees who have defects of a serious nature, those over sixty years of age and those who are exposed to an industrial hazard should receive a periodic examination at least annually. Careful notes are made at these examinations and further investigations should be made if indicated.

The original examination and all subsequent examinations are recorded on a special form or on the face of a folder which contains the other medical records of the employee.

In large factories the examining physician frequently classifies applicants or workers as A, B, C and D or 1, 2, 3 and 4. A Class A worker may work anywhere, as may one in Class B. Class B indicates a number of minor physical defects which should be corrected. Class C indicates that the man should work only in certain departments and at special types of work. He should not be transferred to other work or to another department without the consent of the medical department. Class D means that the man is unfit for work and should not be employed. Such a classification is of special value in large factories where the letter or number tells the employment department the result of the physical examination from an employment standpoint.

From the above it is obvious that the physician examining industrial workers must be familiar with the different kinds of work required in the factory and the physical type of worker best fitted for each department and must have a knowledge of those departments in which there is an industrial health hazard.

It will be seen from this résumé that the physical examination is the first step in medical supervision of the group of workers whose health is the responsibility of the industrial medical department.

W. IRVING CLARK, M.D., *Chairman*
LOUIS R. DANIELS, M.D.
NOEL G. MONROE, M.D.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning December 4.

BARNSTABLE

Sunday, December 10 at 4:00 p.m. at the Cape Cod Hospital Hyannis. Head and Spine Injuries. Instructor: Donald Munro. Donald E. Higgins, *Chairman*.

BRISTOL NORTH

Thursday, December 7 at 4:00 p.m. at the Morton Hospital Taunton. Common Problems of Neurology. Indications for lumbar puncture. Instructor: H. Houston Merritt. Lester E. Butler, *Chairman*.

BRISTOL SOUTH (New Bedford Section)

Friday, December 8 at 4:00 p.m., at St. Luke's Hospital New Bedford. Gonorrhea in the Female. Instructor: Sylvester B. Kelley. Robert H. Goodwin, *Chairman*.

ESSEX NORTH

Friday, December 8 at 4:30 p.m., at the Lawrence General Hospital Lawrence. Convulsions in Infants and Children. Etiology and treatment. Instructor: R. Cannon Eley. John Parr, *Chairman*.

ESSEX SOUTH

Tuesday, December 5 at 4:00 p.m. in the Conference Room of the Salem Hospital Salem. Cardiovascular Disease. Eleven important questions about heart disease and their answers. Instructor: Howard B. Sprague. J. Robert Shaughnessy, *Chairman*.

MIDDLESEX EAST

Tuesday, December 5 at 4:00 p.m. at the Melrose Hospital Melrose. Pneumonia. Instructor: Chester S. Keefe. Walter H. Flanders, *Chairman*.

MIDDLESEX NORTH

Friday, December 8 at 4:45 p.m., at St. John's Hospital Lowell. Cardiovascular Disease. Eleven important questions about heart disease and their answers. Instructor: C. Edward Leach. William S. Lawler, *Chairman*.

WORCESTER (Milford Section)

Tuesday, December 5 at 8:30 p.m., in the Nurses Home of the Milford Hospital Milford. Cardiovascular Disease. Eleven important questions about heart disease and their answers. Instructor: Samuel A. Levine. Joseph Ashkins, *Chairman*.

WORCESTER (Worcester Section)

Friday, December 8 at 8:00 p.m., in the Staff Room of the Worcester City Hospital Worcester. Syphilis in Pregnancy and the Offspring. Instructor: C. Guy Lane. George C. Tuller, *Chairman*.

WORCESTER NORTH

Friday, December 8 at 4:30 p.m., in the Nurses

Home of the Burbank Hospital, Fitchburg Tuberculosis in Infancy and Childhood Instructor Clement A. Smith George P. Keaveny, *Chautman*

RESOLUTION

RESOLUTION RELATIVE TO THE DEATH OF HARVEY CUSHING

The following resolution was passed by the Board of Trustees of the Boston Medical Library at a meeting held on November 20

By the death of Harvey Cushing on October 7, 1939, the Boston Medical Library lost one of its most devoted members. He became a member of the library in 1912, soon after his arrival in Boston to occupy the Moseley professorship of surgery at Harvard and to become the surgeon-in-chief at the Peter Bent Brigham Hospital. Many years before this, however, Cushing had an intimate acquaintance with the library. There is no doubt that he "looked in" as a house pupil at the Massachusetts General Hospital in 1895 and 1896, for 19 Boylston Place was the kind of refuge that Cushing would have found and Brigham and Chidwick the sort of men he was anxious to know. In the new building, moreover, on January 19, 1903, he read one of his early, important papers—a contribution which marked the beginning of blood pressure determinations in this country.

From 1912 to 1932, Cushing was an almost constant user of this library. Although he rarely came to the library himself, except to attend a meeting or chat for a moment with Mr. Ballard, books and journals flowed freely and, at times, almost weekly from Miss McCrea's desk to the hospital and back. Many a carefully prepared list was brought down by the faithful Gus, his chauffeur, only to be filled and carried back in armfuls. How the doctor found time to read so many books was beyond Gus, but back and forth they went, only checked when Cushing took overseas duty from 1917 to 1919. Miss McCrea was an old friend, not forgotten after a period of particularly hard work. In the twenty years he was in Boston, Cushing wrote nine or ten important monographs, and papers too numerous to mention. Did anyone ever use the library more, or to better advantage? He acknowledged his 'deep obligation' to the library in a graceful tribute published in 1926.

This is not the place to evaluate his position in American medicine. He was 'the most distinguished of all surgeons in operative procedures on the brain, a scholar, a biographer, a bibliophile and an outstanding leader of the medical profession. He loved books, encouraged librarians and added to an American collection a notable library of his own. His influence was widely felt and many libraries owe him a profound debt of gratitude for his exemplification of all that books stand for.' In the passing of the only honorary fellow of the Boston Medical Library we are keenly conscious that he is no longer in our midst.

MISCELLANY

NOTES

The following appointments to the teaching and research staff of the Harvard Medical School, effective as of September 1, 1939, were recently announced:

Walter J. E. Carroll, M.D., Jefferson Medical College '28, of Arlington, as assistant in laryngology, Joseph Lettine, M.D., Tufts College Medical School '32, of Milton, as assistant in laryngology, Burton E. Lovesey, M.D., Medico-Chirurgical College of Philadelphia '16, of Boston, as assistant in laryngology, Joseph T. Walker, Ph.D., Harvard '33, of Cambridge, as assistant in legal medicine, Birgit Vennesland, Ph.D., University of Chicago '38, of Chicago, as research fellow in biological chemistry, Robert H. Williams, M.D., Johns Hopkins '34, of Corinth, Mississippi, as research fellow in medicine, Arthur M. Doyle, M.D., University of Toronto '31, of Kingston, Ontario, Canada, as research fellow in neurology, Morley G. Whillans, M.D., University of Toronto '35, of Toronto, Ontario, Canada, as research fellow in neurology, Jürgen Ruesch, M.D., University of Zurich '35, of Brighton, as research fellow in neuropathology, Juan P. Picena, M.D., University of Rosario, Argentina, '32, of Rosario, Argentina, as research fellow in pathology, Joshua C. Drooker, M.D., Tufts College Medical School '33, of Boston, as assistant in laryngology, Walter L. McClintock, M.D., Jefferson Medical School '32, of Quincy, as assistant in laryngology, Frank M. Wattles, M.D., Emory University '33, of Belmont, as assistant in laryngology. In addition, Morris B. Flanagan, M.D., Tufts College Medical School '34, of Dorchester, was appointed assistant in psychiatry, effective January 1, 1940.

Dr. George R. Minot, professor of medicine, Harvard Medical School, has been awarded the Gordon Wilson Medal of the American Clinical and Climatological Association. The presentation took place at a recent meeting of the association at Saranac Lake, New York, at which time Dr. Minot delivered the Gordon Wilson Lecture.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1939

DISEASES	OCTOBER 1939	OCTOBER 1938	FIVE YEAR AVERAGE*
Anterior poliomyelitis	21	5	56
Chick enpox	333	390	347
Diphtheria	24	18	28
Dog bite	827	775	745
Dysentery bacillary	164	19	8
German measles	40	11	31
Gonorrhea	474	416	529
Lobar pneumonia	157	233	241
Measles	291	236	169
Meningococcus meningitis	5	5	7
Mumps	91	204	207
Paratyphoid B fever	3	4	1
Scarlet fever	180	275	407
Syphilis	464	400	441
Tuberculosis pulmonary	239	232	275
Tuberculosis other forms	24	35	34
Typhoid fever	4	2	10
Undulant fever	4	1	5
Whooping cough	347	375	431

*Based on figures for preceding five years

RARE DISEASES

Anterior poliomyelitis was reported from Boston, 4, Braintree, 1, Clinton, 1, Dudley, 1, Fall River, 2, Foxboro, 1, Haverhill, 1, Holbrook, 1, Lynn, 1, Somerville, 1, Wareham, 1, Watertown, 1, Winchester, 1, Worcester, 4, total, 21.

Diphtheria was reported from Boston, 5, Cambridge, 3, Fall River, 4, Foxboro, 2, Lawrence, 3, Malden, 1, Methuen, 1, Somerville, 1, Wakefield, 2, Worcester, 1, Wrentham, 1, total, 24.

Dysentery, bacillary, was reported from Boston, 9, Cambridge, 11, Duxbury, 3, Dedham, 1, Fall River, 3, Framingham, 1, Lowell, 5, Medfield, 24, Medford, 1, Northampton, 1, Northboro, 1, Palmer, 1, Waltham, 9, Watertown, 5, Worcester, 2, Wrentham, 87, total, 164.

ectious encephalitis was reported from Holden, 1
 1.
 meningococcus meningitis was reported from Berlin 1
 River 1 Fitchburg 1 Plymouth 1 Wellesley 1
 5
 typhoid B fever was reported from Cambridge, 1
 it, 1 Lynn 1 total 3
 lagra was reported from Boston 1 total 1
 dter bacillus meningitis was reported from Arlington
 total, 1
 sore throat was reported from Arlington, 1
 n, 4, Brockton 1 Cambridge, 2 Greenfield 1 Mil-
 1 total, 10
 anus was reported from Billerica 1 Westfield, 1
 2.
 dthoma was reported from Boston 2 total 2.
 dthosis was reported from Fall River 2 total 2.
 d fever was reported from Belmont, 1 Boston, 2
 ry 1 total, 4
 ulant fever was reported from Great Barrington, 1
 ale, 1 Montague 1 North Reading 1 total 4

lary dysentery continues to be reported to an un-
 r high level.

the fourth consecutive month the reported incidence
 ar pneumonia reached its lowest level for the past
 ars.

reported incidences of anterior poliomyelitis and
 goccoccus meningitis were within normal limits.
 ngs and scarlet fever continued to be reported at very
 vels.

reported incidences of diphtheria, typhoid fever
 atyphoid B fever were encouragingly low
 onary tuberculosis, tuberculosis (other forms) and
 nt fever were reported within the five year average.
 reported incidences of chickenpox measles, German
 s, and whooping cough were not remarkable.
 the third consecutive month the reported incidence
 bite reached a new high for the month

RESPONDENCE

APPROVING AUTHORITY

the Editor In accordance with the vote of the Ap-
 roving Authority on September 28 1939 I enclose for
 information a copy of the circular letter with cir-
 cular information and the law creating the Approving
 Authority in Massachusetts to be sent to every medical
 school in the United States and Canada to all state boards
 of registration to certain medical journals and to the press.

STEPHEN RUSHMORE, M.D., *Chairman*
 Approving Authority

Boston, Boston.

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COPY OF CIRCULAR LETTER FROM THE APPROVING AUTHORITY

attention is called to the enclosed copy of the
 Massachusetts statute creating an approving authority for
 universities and medical schools, which will be
 effective on January 1 1941 for the rejection of
 licenses for examination for registration as qualified
 persons on the ground of graduation from a non-
 approved school. There is enclosed also a circular of in-
 formation concerning general requirements for approval
 of universities and medical schools.

In the evaluation of medical schools outside of Massa-
 chusetts, the Approving Authority will in general give due
 weight to the evaluation of such schools by the board of
 registration in medicine, or equivalent body of the state
 in which the school is situated.

Nothing however in this letter or in the accompanying
 circular of information is to be interpreted as waiving the
 right of the Approving Authority to include in the basis
 for its decision concerning a college, university or medi-
 cal school evidence disclosed by its own investigations

MIDDLESEX UNIVERSITY SCHOOL OF MEDICINE

To the Editor I have been approached by the Graduate
 Association of the Middlesex University School of Medi-
 cine to state the terms under which I would serve as a
 trustee of their school. My statement was as follows

My sole object in bringing up the subject of the Middle-
 sex University School of Medicine for discussion is to im-
 prove in the immediate future the qualifications of its
 graduates who are to practice in Massachusetts

If the medical school will meet the following require-
 ments and the Governor of the Commonwealth and the
 Council of the Massachusetts Medical Society will agree
 each to appoint one seventh of the trustees, then I would
 accept membership on its Board of Trustees.

The requirements are.

1. *New Fund of \$100,000* The alumni of the
 school must show their confidence in it by securing
 funds for its immediate needs before either they or
 the school can expect anyone else to take an active
 interest. Therefore, the first condition is that \$100,000
 be pledged and of this, \$30,000 in cash deposited in
 a bank before February 1, 1940. \$30,000 pledged to be
 deposited in cash by July 20 1940. \$40,000 pledged to
 be deposited in cash by January 20 1941. The money
 should be obtained with the understanding that it is
 to be expended wholly in addition to present current
 expenditures and with the general approval of the
 Graduate Association of the Middlesex University School
 of Medicine and as follows

- (a) \$15,000 spent on instruction including library
 and equipment, for the benefit of the first
 two-year classes before July 1 1940
- (b) \$40,000 likewise expended during the school
 year 1940-1941 but to be distributed accord-
 ing to the needs of the entire four years.
- (c) \$45,000 similarly to be expended during 1941
 1942.

It is recognized that these expenditures do not meet
 what is necessary but they should bring about a rela-
 tively marked improvement in the education of the
 students.

2. *Valuation of the Property* The value of the
 school property should be determined. Whether the
 land and buildings are worth \$300,000 or \$1,000,000
 I do not know but the assessed value should be con-
 sidered and what the actual value would be if the
 entire property were put up for sale. For example
 the library may have books which originally cost
 \$30,000 but today if put at auction might not bring
 \$1000 consequently the value of the library as every-
 thing else in the school should be estimated by its
 salable value. Such total valuation within the limits
 of \$100,000 should be easily made by an expert from
 the First National Bank, the Boston Safe Deposit and

Trust Company, the State Street Trust Company or any large banking institution in good standing

3 *The Debt Funded and Held by Responsible Organizations* That the debt of the school shall be funded and the loan held by one, two or three responsible organizations, just as at a certain Boston hospital all its debts are funded in one sum by an arrangement with a large life insurance company, and that the rate of interest shall not exceed 4 per cent.

4 *Yearly Publications of Finances* In accordance with the custom of charitable institutions incorporated in the Commonwealth a complete financial statement shall be published annually

5 *Limitation of Students* Limitation of students, after this school year, 1939-1940, to an entering class of 75 with the understanding that no one of the remaining three classes shall exceed this number except in the next three years if this is necessary to accommodate those now enrolled in the first, second and third years

6 *Anatomical and Clinical Facilities* That anatomical facilities shall be assured and that a hospital or hospitals shall indicate that, when all the foregoing conditions are met, they will make 200 beds in their institution or institutions available for the clinical instruction of Middlesex medical students

7 *Composition of Board of Trustees* That one seventh of the Board of Trustees shall be chosen by graduates of the school licensed to practice in Massachusetts, one seventh by the Governor of Massachusetts, one seventh by a committee appointed by the Council of the Massachusetts Medical Society, each for five year terms, and the remaining four sevenths by the present or then existing Board of Trustees of the Middlesex University School of Medicine and that either none or not more than one seventh of the trustees shall be members of the faculty, with the understanding that no faculty member shall have voting power

Unhesitatingly I believe that, if the conditions above set forth are met, the education of the students of the school will be so advanced that it will deserve and receive further support in all ways

I append the reply of the Graduate Association of the Middlesex University School of Medicine to my statement.

ELLIOTT P JOSLIN

81 Bay State Road,
Boston

* * *

Dr Elliott P Joslin

The Graduate Association of the Middlesex University School of Medicine accepts your requirements in so far as it is empowered to act. Upon the acceptance by the university of the parts of the contract pertaining to the medical school, the association will fulfill the new fund contract as set aside in Part I

In behalf of the graduates of the Middlesex University School of Medicine we extend to you our thanks for your aid in our efforts toward obtaining approval of our school

HAROLD L. MUSGRAVE, *President*,
M L. KRAFT, *Secretary*
Graduate Association, Middlesex University
School of Medicine.

REPORT OF MEETING

THE THIRD INTERNATIONAL NEUROLOGICAL CONGRESS

The Third International Neurological Congress was held at Copenhagen, Denmark, August 21 to 25, 1939, with an attendance of about 500 physicians from all parts of the world. In spite of the unrest in Europe at the time, there were representatives at the Congress from all countries. Most of the delegates remained until the last day, only the English delegation felt it incumbent upon themselves to leave the Congress before the sessions were over. The meetings were held at the University of Copenhagen and the Congress was opened by His Majesty the King of Denmark in an impressive ceremony on August 21. The scientific sessions began the same day and the topic "The Endocrine-Vegetative System with Special Reference to Neurology" was considered. On Tuesday, August 22, the topic was "The Heredofamilial Diseases, Especially from the Genetic Aspect." Both these topics were discussed by special reporters and, in addition, there were numerous papers by members of the Congress. On Thursday, August 24, the Congress was resumed, after a day given to entertainment. On that day the Congress was divided into various sections and a large number of papers were read on anatomy and pathology, clinical neurology, therapy, epilepsy and neurosurgery. On Friday, the last day, the topic "Neurological Aspects of the Avitaminoses with Special Reference to the Peripheral Nervous System" was considered by a group of special reporters and also in a series of papers by other members of the Congress. In general the papers were of high quality, particularly the reviews submitted by the special reporters on topics which had been chosen in advance.

Of the many papers, a few deserve special mention. Sir Henry H. Dale, of London, summarized his work in a paper entitled "Chemical Mediation in the Peripheral Nervous System and Its Relation to Endocrine Organs." He believes that acetylcholine serves as a transmitter of the excitatory process at the ganglionic synapses and at the motor nerve endings in voluntary muscles. At the pre-ganglionic synapse, acetylcholine acts on the parasympathetic system, as well as the sympathetic system, as the chief transmitter. On the other hand, the postganglionic synapse is partly served by acetylcholine. Adrenaline, on the other hand, does not serve as a transmitter for voluntary impulses, but does almost exclusively serve at the pre-ganglionic sympathetic synapse and rarely at the pre-ganglionic parasympathetic synapse. It is also held at the endings of most of the postganglionic fibers of the sympathetic system. The method of disappearance of acetylcholine after its liberation, with such speed as to be completely within the refractory period of the ganglion cell or muscle fiber, is a point of uncertainty. In the case of voluntary muscles it can be shown that depression of the cholinesterase action by physostigmine or Prostigmin causes a single motor nerve to go into tetanus. It seems most probable that the function of the cholinesterase at the nerve ending is to prevent excess of acetylcholine liberated by an impulse from producing depression, rather than to secure its complete removal during the refractory period. Some other mechanism seems to be required for this. Another paper was on the anatomy of the cerebral and bulbospinal sections of the autonomic nervous system by Dr Laruelle, of Brussels. The author demonstrated by a series of excellent charts the details of this system, his researches having brought to light considerable new material based on a study of longitudinal sec-

ions of the nervous system rather than that of the usual root sections. Dr John F. Fulton of New Haven Conn. spoke on "Central Levels of Autonomic Function, with Particular Reference to the Cerebral Cortex and the Endocrine Organs" paying special attention to the hypothalamic level and that of the cerebral cortex. The autonomic function of the hypothalamic region is closely associated with the innervation of the pituitary gland and the control of the kidney through the posterior lobe hormone, and the regulation of thyroid, adrenocortical and ovarian activities through the anterior lobe hormone. The regulation of body temperature, moreover is controlled from the hypothalamus. This level is under direct control of the cortex, and thus it seems reasonable to assume that the cerebral cortex plays an intimate part in regulating the activity of the endocrines, as does the hypothalamus itself. It has already been shown that the adrenal medulla can be made to secrete as the result of stimulation of the renal lobes.

Sir Edward Mellanby of London summarized his views on the neurological aspects of the avitaminoses. Nicotinic acid acts as the pellagra preventing factor but also has an effect on the central and peripheral nerve lesions of this disease. It appears to be particularly useful in the treatment of the psychotic states associated with pellagra. It is also probable that vitamin B₆ and vitamin A will both prove to be of value in treating neurologic conditions. In addition there is the well known effect of vitamin B₁ and lack of it probably prevents proper nerve function largely because it interferes with carbohydrate oxidation a type of metabolic process on which the nervous tissue is unusually dependent. Dr Israel S. Wechsler of New York, emphasized that many cases of polyneuritis probably represent true deficiency syndromes and belong to the class of avitaminoses. He even suggested that polyneuritis due to arsenic, diabetes or phosphorus might be on the same basis. Dr Wechsler's point of view was borne out by Dr Charles C. Ungley of Newcastle, England. He stated that in the majority if not all, of thirty-six cases of polyneuritis avitaminosis it was probably responsible for the chief symptoms. It did not appear however to be an important factor in diabetic neuritis or neuritis due to gout, lead diphtheria toxin or certain unexplained causes. Dr H. P. Stubbe Teglbjaerg of Denmark, gave an excellent summary of the treatment of various nervous disorders with vitamin B₁. He advocated its use in all cases of peripheral neuritis irrespective of etiology. The body probably requires 1 to 2 mg. per day by mouth of vitamin B₁ but during pregnancy lactation, fever hyperthyroidism and other pathologic conditions this amount should be increased five to ten times. The greatest effect is obtained when the vitamin is given intravenously. Overdosage does not appear to cause injury.

The Surgical Section of the Congress met on Thursday August 24. In the absence of Mr Geoffrey Jefferson, of Manchester England, Dr W. Jason Mixter of Boston, presided. In general the character of the papers was excellent. Particular reference should be made to the paper by Dr E. Busch, of Copenhagen on traumatic epilepsy that by Dr Erik Lysholm of Stockholm, on ventriculography that by Dr Arne Torkildsen, of Oslo, on occlusion of the Sylvian aqueduct and that by Professor H. Olivecrona of Stockholm on the acoustic neuroma. It was unfortunate that a number of distinguished neurosurgeons on the program were prevented from being present by the tense international situation.

The members of the Congress were entertained in a generous manner by their colleagues in Scandinaviania. There was an official reception on Sunday August 26 a banquet in the Town Hall on Monday and excursions to

the Castles of Kronborg and Frederiksborg on Wednesday with the official banquet of the Congress on Thursday evening. In addition there were many informal dinners given by the Danish neurologists to the various delegates. The only honorary president of the Congress present was Dr Gordon Holmes, of London. The president was Professor Viggo Christensen of Copenhagen, long a leader in neurology and practically the founder of neurology as a specialty in Copenhagen. He was ably assisted by his Scandinavian colleagues, Professor Antoni of Sweden, Professor Fabritius of Finland and Professor Monrad-Krohn, of Norway and by the secretary general Dr K. H. Krabbe, of Copenhagen.

The Congress served to join together through their common interests many of the leading neurologists of the Continent and America. No one who attended this Congress so skillfully arranged under the impending threat of a European war could leave Copenhagen without a feeling of sincere sympathy for friends who were soon to be caught in a conflict not of their own choosing. It was indeed fortunate that the Congress could be held in Copenhagen and that its sessions were completed a week before war broke out.

It will be of particular interest to the readers of the *Journal* to know that the following twelve papers* were presented by members of the Congress from the New England states.

- Dr John F. Fulton (New Haven) Central Levels of Autonomic Function with Particular Reference to the Cerebral Cortex and the Endocrine Organs.
- Dr Abraham Myerson (Boston) Human Autonomic Pharmacology.
- Drs. Henry R. Viets and Robert S. Schwab (Boston) Myasthenia Gravis A historical and clinical motion picture.
- Drs. Robert S. Schwab and Henry R. Viets (Boston) Myasthenia Gravis Clinical observation of fifty cases.
- Drs. Madeline R. Brown and John H. Talbott (Boston) The Role of Potassium Chloride in the Treatment of Ménière's Syndrome.
- Drs. W. G. Lennox, E. L. Gibbs and F. A. Gibbs (Boston) The Inheritance of Epilepsy as Revealed by the Electroencephalograph.
- Drs. H. Houston Merritt and Tracy J. Putnam (Boston) On Diphenyl Hydantoin and Other New Anticonvulsant Drugs.
- Drs. William J. German and Max Taffel (New Haven) Surgical Production of Collateral Intracranial Circulation An experimental study.
- Drs. W. Jason Mixter and Joseph S. Barr (Boston) Rupture of the Lower Lumbar Intervertebral Disks.
- Dr. Leo Alexander (Boston) Ben Berli and Wernicke's Hemorrhagic Pseudoencephalitis An experimental study.
- Dr. Tracy J. Putnam (Boston) The Treatment of Athetosis by Section of Extrapyramidal Tracts. (Read by title.)
- Dr. James L. Poppen (Boston) Sphenoid Ridge Meningioma en plaque Surgical technic. (Read by title.)

* Full list of 11 the papers given at the Congress have been published in booklet form under the title *III International Neurological Congress Copenhagen 1939* Munksgaard, 1939.

NOTICES

ANNOUNCEMENT

HERMAN BEIGELMAN M.D., announces the opening of an office at 36 Quincy Avenue, East Braintree.

REMOVAL

REGINALD D MARGESON, M.D., announces the removal of his office to 1101 Beacon Street, Brookline

BOSTON DOCTORS
SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide, former concert-master with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, every

Thursday at 8 30 p.m., in Studio A, Station WMEX, 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430)

JOSEPH H PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Auditorium, 9 10 a.m.

MEDICAL CONFERENCE PROGRAM

- Friday, December 1 — A Psychology of the Hard of Hearing Mr C G Loring
Saturday, December 2 — Hospital Case Presentation Dr S J Thannhauser
Tuesday, December 5 — Diagnosis and Treatment of Internal Derangements of Knee Joints Dr John D Adams
Wednesday, December 6 — Hospital Case Presentation Dr S J Thannhauser
Thursday, December 7 — Auricular Conduction in the Mammalian Heart. Dr Emanuel Ginsburg
Friday, December 8 — Recent Studies on Liver Disease Dr Franklin W White.
Saturday, December 9 — Hospital Case Presentation Dr S J Thannhauser
Tuesday, December 12 — Some Ophthalmoscopic Signs in Constitutional Disease. Dr Joseph J Skirball
Wednesday, December 13 — Hospital Case Presentation Dr S J Thannhauser
Thursday, December 14 — Gastrointestinal Clinic Presentation of cases Dr K S Andrews
Friday, December 15 — Sir James Mackenzie General practitioner Dr Joseph H Pratt.
Saturday, December 16 — Hospital Case Presentation Dr S J Thannhauser

Medical conferences will be resumed Tuesday morning, January 2, 1940

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, December 6, from 2 to 4 p.m. Drs Stanley Emory and Robert Zollinger will speak on "Diarrhea and Constipation." A clinicopathological conference, conducted by Dr Elliott C Cutler, will take place from 4 to 5 p.m.

On Thursday, December 7, from 8 30 to 9 30 a.m. there will be at the Peter Bent Brigham Hospital, a combined clinic, conducted by Dr Soma Weiss, of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C CUTLER, M.D., *Secretary*

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, December 5, at 8 15 p.m.

Dr Emil Novak, associate professor of obstetrics, University of Maryland, will speak on "Gynecological Endocrinology and Organotherapy." Discussion by Drs. Joseph C Aub, Max Davis and Samuel L Gargill

MAX RITVO, M.D., *President*,
D B STEARNS, M.D., *Secretary*

FAULKNER HOSPITAL
CLINICOPATHOLOGICAL CONFERENCE

The monthly clinicopathological conference of the Faulkner Hospital will be held on Thursday, December 7, at 5 00 p.m. Dr Maxwell Finland will speak on "Chemotherapy and Serotherapy in Pneumonia."

Interested members of the medical profession are invited to attend

WALTHAM MEDICAL MEETINGS

The following medical meetings will be held in Waltham during December

WALTHAM HOSPITAL

- December 8 Staff Meeting — 8 30 p.m.
December 15 Clinicopathological Conference — 8 30 p.m.
December 22 Waltham Medical Club Meeting — 8 30 p.m.

MIDDLESEX SANATORIUM

- December 4 Clinicopathological Conference — 8 00 p.m.
Staff Conferences every Wednesday at 9 00 a.m. and every Friday at 2 00 p.m.

METROPOLITAN STATE HOSPITAL

- Staff Meetings every Monday, Tuesday, Wednesday and Thursday at 11 00 a.m.
X-Ray Conferences every Wednesday at 2 00 p.m.
Neurological Conferences every Wednesday at 3 00 p.m.
December 27 Clinicopathological Conference — 8 00 p.m.

WALTER E FERNALD SCHOOL

- Outpatient Clinics every Wednesday morning
Staff Meetings every Thursday morning

All interested physicians are cordially invited to attend any of these meetings

UNITED STATES MARINE HOSPITAL

The staff meeting of the United States Marine Hospital, Chelsea, Massachusetts, will be held at "The Hut," on Wednesday afternoon, December 6, at 4 00

PROGRAM

- The Clinical and Laboratory Aspects of Fungous Infections John G Downing, M.D.

JOHN W TRASK, *Medical Director in Charge*

INTERNATIONAL COLLEGE
OF SURGEONS

The New England Section of the International College of Surgeons will hold a Postgraduate Study Guild at the

field State Sanatorium Cancer Section on Wednesday, December 13.

PROGRAM

10 to 12 m

Stomach Surgery Case. Dr. E. M. Daland
 Late-Stage Abdominoperineal Operation for Carcinoma
 of Rectum. Dr. F. H. Baehr
 Abdominal Gastric Cancer of stomach. Dr.
 E. W. Beauchamp
 Urinary Case. Dr. A. J. Connelly

10 to 4.30 p.m.

Year End Results of Breast Cancer at Pondville
 Hospital. Dr. E. M. Daland.
 Attitude toward Cancer of the Breast. Dr. E. W.
 Beauchamp.
 Presentation of Three Cases of Malignant Melanoma.
 Dr. F. H. Baehr
 Metastatic Malignancies of the Lungs and Skeleton.
 Dr. J. W. Turner
 Obstetrical Complications of Carcinoma of Cervix and
 Rectum. Dr. J. A. Seaman
 Experience with Diagnosis and Treatment of the
 Leukemias. Dr. J. E. Dwyer
 Metastatic Sarcoma. Dr. R. M. Fienberg
 Antemortem Recognition of Fatal Pulmonary
 Embolism. Dr. A. S. Johnson.
 Choice of Operations for Rectal Malignancies. Dr.
 F. S. Hopkins.
 Treatment of Cancer of the Vulva. Dr. A. J.
 Douglas.

Paul J. Jakmau, Massachusetts commissioner of
 health will give an address of welcome in open
 afternoon program. Dr. George S. Foster of
 New Hampshire, will preside. Luncheon
 served to guests. All physicians are cordially

MEETINGS AND CONFERENCES

MEETING OF BOSTON DISTRICT FOR THE WEEK BEGINNING
 13, DECEMBER 4

DECEMBER 4
 5 p.m.-11.15 p.m. Clinicopathological conference. Dr. S. Burt
 Kohnsaw, Peter Bent Brigham Hospital amphitheater
 m. Physicians and medical students are cordially invited to attend
 a clinic presented by the medical, surgical and orthopedic services
 of the Infants and Children's Hospital in the amphitheater of the
 Children's Hospital.

DECEMBER 5
 10 a.m. Diagnosis and Treatment of Internal Derangements of Knee
 Joints. Dr. John D. Adams, Joseph H. Pratt Diagnostic Hospital
 10 a.m.-12.30 p.m. Boston Dispensary tumor clinic
 5 p.m.-11.15 p.m. X-ray conference. Dr. Merrill C. Sommer.
 Peter Bent Brigham Hospital amphitheater
 8 p.m. Massachusetts Hospital Association. Parker House, Boston
 8 p.m. Greater Boston Medical Society. Auditorium, Beth Israel
 Hospital

DECEMBER 6
 10 a.m. Obstetrical and Gynecological Society
 10 a.m. Hospital case presentation. Dr. S. J. Thalhauer
 Joseph H. Pratt Diagnostic Hospital
 10 a.m. Clinicopathological conference. Children's Hospital amphitheater
 10-11 p.m. Joint medical and surgical clinic. Peter Bent Brigham
 Hospital

DECEMBER 7
 10-11.30 a.m. Combined clinic of the medical surgical ortho-
 pedic and pediatric services of the Children's Hospital and the
 Peter Bent Brigham Hospital at the Children's Hospital.
 10 a.m. Arterial Conduction in the Mammary Heart. Dr.
 Samuel G. Loring. Joseph H. Pratt Diagnostic Hospital

5 p.m. Fulkner Hospital clinicopathological conference.
 7 p.m. New England Hospital for Women and Children. Clinical
 conference and meeting of staff
 FINE DISEASES
 49-10 a.m. Recent Studies on Liver Disease. Dr. Franklin W. White.
 Joseph H. Pratt Diagnostic Hospital.
 10 a.m.-12.30 p.m. Boston Dispensary tumor clinic
 8 p.m. W. H. W. Society. Auditorium, Beth Israel Hospital.

5 p.m. DISEASES
 49-10 a.m. Hospital case presentation. Dr. S. J. Thalhauer
 Joseph H. Pratt Diagnostic Hospital
 10 a.m.-12 m. Medical staff rounds of the Peter Bent Brigham Hos-
 pital. Conducted by Dr. Sooma Weiss.

*Open to the medical profession.

DECEMBER 11—Boston Dispensary. "The Psychology of the Hard of Hear-
 ing." Mr. John C. O. Loring. Page 440, issue 1 November 23
 DECEMBER 12—Joseph H. Pratt Diagnostic Hospital. Medical Confer-
 ence Program. Page 880
 DECEMBER 12—America. Board of Obstetrics and Gynecology. Page 1019
 issue of June 15
 DECEMBER 14—Middlesex Sanatorium. Clinicopathological conference. Page
 880
 DECEMBER 15—Massachusetts Hospital Association. Page 798, issue of
 November 16
 DECEMBER 15—Greater Boston Medical Society. Page 880
 DECEMBER 16—Peter Bent Brigham Hospital. Joint medical and surgical
 clinic. Page 880
 DECEMBER 16—United States Marine Hospital. Staff meeting. Page 880
 DECEMBER 16—Wachusett Medical Improvement Society. Page 798, issue
 of November 16
 DECEMBER 16—New England Obstetrical and Gynecological Society. Page
 799, issue of November 9
 DECEMBER 17—Combined clinic of the medical surgical orthopedic and
 pediatric services of the Children's Hospital and the Peter Bent Brigham
 Hospital. Page 880
 DECEMBER 17—Fulkner Hospital clinicopathological conference. Page 880
 DECEMBER 17—New England Hospital for Women and Children. Page
 841, issue of November 23
 DECEMBER 18—William Harvey Society. Page 676, issue of October 26
 DECEMBER 18—W. H. W. Society. Staff meeting. Page 880
 DECEMBER 18—International College of Surgeons. Page 880
 DECEMBER 18—Pennsylvania Association of Physicians. 8.30 p.m., Hotel
 Butler, Haverhill
 DECEMBER 18—W. H. W. Hospital. Clinicopathological conference. Page
 880
 DECEMBER 22—W. H. W. Medical Club. Page 880
 DECEMBER 22—Metropolitan State Hospital. Clinicopathological confer-
 ence. Page 880
 JANUARY 6, 1940—America. Board of Obstetrics and Gynecology. Page 1606,
 issue of July 27 and page 798, issue of November 16.
 JANUARY 6, 1940—American Academy of Orthopedic Surgeons.
 Hotel Statler, Boston.
 FEBRUARY 11-14—International College of Surgeons. Page 799, issue
 of November 9
 MARCH 2, 1940—American Board of Ophthalmology. Page 719,
 issue of November 2.
 MARCH 7-9, 1940—The New England Hospital Association. Hotel Statler,
 Boston.
 MAY 14, 1940—Pharmacological Convention. Page 894, issue of May 25.
 JUNE 7-9, 1940—American Board of Obstetrics and Gynecology. Page
 1019, issue of June 15

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 3, 1940—Semi-annual meeting. Combined meeting with Essex
 South. Danvers State Hospital. 7 p.m.

ESSEX SOUTH

DECEMBER 6—"Typhoid Fever and Its Relation to Other Infectious
 Diseases of the Kidney." Dr. Sooma Weiss. Salem Hospital, Salem.

JANUARY 3, 1940—"Lead Poisoning." Dr. John S. Hodgson. Danvers
 State Hospital, Haverhill.

FEBRUARY 14—"Cough Spasms, Hemoptysis—How shall they be treated?"
 Dr. Reece H. Betts. Essex Sanatorium, Middlesex.

MARCH 6—"Experimental and Clinical Consideration of Sulfanilamide
 Treatment of Hemolytic Streptococcal Infection." Dr. Champ Lyman.
 Lynn Hospital, Lynn.

APRIL 5—Addison Gilbert Hospital, Gloucester

MAY 8—Annual meeting. Salem Country Club, Peabody

HAMPSHIRE

JANUARY 10, 1940

MARCH 13

MAY 8.

All meetings are held at 11.30 a.m. at the Cowley Dickinson Hospital,
 Northampton.

MIDDLESEX EAST

JANUARY 10 1940

MARCH 20

MAY 15

Meetings are held at 12 15 p.m. at the Unicorn Country Club Stoneham

MIDDLESEX NORTH

JANUARY 31 1940

APRIL 24

JULY 31

OCTOBER 30

NORFOLK SOUTH

DECEMBER 7

JANUARY 4 1940

FEBRUARY 1

MARCH 7

APRIL 4

MAY 2

All meetings, with the exception of one which is usually held at the Quincy City Hospital are held at the Norfolk County Hospital in South Braintree at 12 o'clock noon

PLYMOUTH

JANUARY 18 1940 — Brockton Hospital Brockton

MARCH 21 — Goddard Hospital Brockton

APRIL 18 — State Farm.

MAY 16 — Lakeville Sanatorium Lakeville

SUFFOLK

JANUARY 31 1940 — Scientific meeting Subject to be announced later

MARCH 27 — Scientific meeting Symposium on Ulcerative Colitis and Diarrheas Under the direction of Dr Chester M Jones

APRIL 24 — Annual meeting in conjunction with the Boston Medical Library Election of officers Program and speakers to be announced later

WORCESTER

DECEMBER 13 — St Vincent Hospital

JANUARY 10 1940 — Worcester City Hospital

FEBRUARY 14 — Worcester State Hospital

MARCH 13 — Worcester Memorial Hospital

APRIL 10 — Worcester Hahnemann Hospital

MAY 8 — Worcester Country Club

Each meeting begins with a dinner at 6 30 p.m. and is followed by a business and scientific meeting

BOOKS RECEIVED FOR REVIEW

Bacteriology Clio Medica 22 William W Ford 207 pp New York and London Paul B Hoeber, Inc., 1939 \$2 50

Facts and Theories of Psychoanalysis Ives Hendrick. Second edition 369 pp New York Alfred A Knopf, 1939 \$3 00

Benzene (Benzol) Poisoning Five papers Reprinted from *The Journal of Industrial Hygiene and Toxicology*, Vol 21, No 8, 1939 114 pp Boston Journal of Industrial Hygiene and Toxicology, 1939 \$1 00

Cancer of the Larynx Chevalier Jackson and Chevalier L. Jackson 309 pp Philadelphia and London W B Saunders Co, 1939 \$8 00

Supervision in Public Health Nursing Violet H Hodgson 376 pp New York The Commonwealth Fund, 1939 \$2 50

In Memoria del Prof Fabio Rivalta Societa Medico-Chirurgica di Romagna 398 pp Faenza, Italy Fratelli Lega, 1939

Studies from the Rockefeller Institute for Medical Research Vol 113 604 pp New York The Rockefeller Institute for Medical Research, 1939 \$2 00

Health in Handcuffs John A Kingsbury 210 pp New York Modern Age Books, Inc., 1939 75c

A Manual for Diabetic Patients W D Sansum, Alfred E. Koehler and Ruth Bowden 227 pp New York The Macmillan Co, 1939 \$3 25

Epidemiology in Country Practice William N Pickles 110 pp Baltimore Williams & Wilkins Co, 1939 \$2 50

An Introduction to Dermatology Norman Walker and G H Percival Tenth edition 391 pp Baltimore Williams & Wilkins Co, 1939 \$7 00

Twilight of Man Earnest A. Hooton 308 pp New York G P Putnam's Sons, 1939 \$3 00

The Physiological Basis of Medical Practice A University of Toronto text in applied physiology Charles Best and Norman B Taylor Second edition 1872 Baltimore Williams and Wilkins Co, 1939 \$10 00.

Tumors of the Hands and Feet Edited by George Pack. 138 pp St. Louis C V Mosby Co, 1939 \$3 00

BOOK REVIEWS

Relation of Trauma to New Growths Medico-legal aspects R. J Behan 425 pp Baltimore Williams & Wilkins Co, 1939 \$5 00

This volume would probably not have been written but for the questions as to the etiology of neoplasms that are all too frequently raised in the courts in connection with the various workmen's compensation laws. As the author points out in his preface, the average physician is only rarely called to testify in such a case and heretofore it has only been with considerable difficulty that he has been able to secure reliable data on the problem. This book should therefore fill a distinct need. All types of neoplasm and the relation of their life history to trauma are reviewed in the thirty chapters. The author has had the assistance of several lawyers in the compilation of the book and it should be as useful to the legal profession as to physicians. There is an excellent bibliography at the end of each chapter.

While this book will hardly be useful in the everyday practice of medicine, it will undoubtedly prove to be invaluable to many physicians who are called to testify on the relation of injury to the etiology or life history of a new growth.

Brucellosis in Man and Animals I Forest Huddleston. 339 pp New York The Commonwealth Fund, 1939 \$3 50

This monograph on brucellosis is an expanded and up-to-date edition of the volume entitled *Brucella Infections in Animals and Man* (1934). The former volume dealt only with bacteriological aspects of the subject. The new monograph presents the important aspects of diagnosis and treatment with considerable thoroughness. The book should prove of inestimable value to practicing physicians and veterinarians, as well as to laboratory workers concerned with *Brucella*.

Roentgen Technique Clyde McNeill 315 pp Springfield, Illinois, and Baltimore Charles C Thomas, 1939 \$5 00

In the reviewer's opinion this is the most concise and at the same time the most complete manual of roentgen technic published to date.

The book is replete with photographs, line drawings, charts and tables for handy reference. The more recent technical procedures of pelvimetry, encephalography, kymography and tomography are described. Authors are credited and references given to the original articles for detailed study.

Not only the roentgen technician but also the roentgenologist will find this book indispensable.

The New England Journal of Medicine

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VOLUME 221

DECEMBER 7, 1939

NUMBER 23

THE PHYSICAL EXAMINATION OF GROUPS

ROBERT W. BUCK, M.D. *

BOSTON

GROUP examination is largely a phenomenon of contemporary society. A generation ago, most the only occasion for a person to submit himself to medical inspection for any reason other than his own inclination was an application for life insurance. At the present time he may be led upon to do so because he is contemplating marriage, entering college, medical school or naval aviation, applying for a barber's or automobile driver's license, or simply as a hygienic duty. The number and variety of groups requiring special types of physical examination are constantly increasing. If these examinations are to serve their purposes adequately, it is necessary for the examining physician to understand clearly the results which it is hoped will be accomplished, and to consider carefully the means best adapted to attain them.

With the development of modern industrial civilization there has come such an increasing intercommunication among large numbers of people, each community of interest and activity, that people function more and more as parts of groups. They naturally do not lose their individual ailments, and continue to require the ministrations of private physicians, but at the same time, as parts of large groups they affect the functioning of these groups, and certain aspects of their health which do not seriously affect them as individuals may definitely affect the functioning of the groups, even endanger the health of large numbers of other people. Thus, a man with a cold in the head may not be ill enough to require the services of a physician, but by going to work in a large factory he may come into personal contact with any people and transmit his benign cold to many of them, as a result a certain number of these affected persons will develop bronchitis, sinusitis, pneumonia or even pulmonary tuberculosis, which they would otherwise have escaped. The handling of the man with a cold thus becomes a problem

of group health. The economic aspects of an epidemic in a large body of employed persons are likewise apparent.

The functions and purposes of the group examination are different from those of the individual physical examination. By and large it may be said that just as the purpose of the latter is diagnosis as a guide to treatment, so the purpose of the group examination is prognosis. In the individual doctor-patient relation the search for a diagnosis leads the examiner to concentrate his attention on a possible disease. Most group examinations, on the other hand, deal with presumably healthy persons, and here the object of attention is the less tangible factor of the individual's capacity to withstand the strain of a disease or of the special hazards incident to a given occupation. A knowledge of pathology is necessary for a correct diagnosis; a knowledge of physiology or the normal range of human capacity, is necessary for a correct prognosis in the sense mentioned.

TESTS OF PHYSICAL FITNESS

Most of those who conduct group examinations accept this problem of prognosis as being one of determining physical fitness. Practically all group examinations start at this point and their basis is the simple physical examination. A man is considered fit if he shows no signs of disease. This might seem adequate for the life insurance examination, although even here other factors soon enter in but it is not a satisfactory criterion for qualifying a man to be an army or navy air pilot. Even the simple physical examination has its prognostic value, however, as may be illustrated by the following experience.

In 1934 I directed the medical examination of 250 members of the police force of a suburban community at the request of the mayor whose primary purpose appeared to be to bring about the discharge of some members who were considered undesirable. In the absence of any other

* Assistant professor of preventive medicine, Tufts College Medical School, senior physician, Boston Dispensary.

guiding standard, I undertook to classify the men in four groups, on the basis of the physical examination routinely given in the Health Clinic of the Boston Dispensary. Group A comprised men with no significant physical defects, of these there were 69. Group B comprised men with one or two minor defects, of these there were 108. Group C comprised men with three or more minor defects, of these there were 33. Group D comprised men with major defects, of these there were 20. The distinction between minor and major defects was quite arbitrary but in view of the results was apparently sufficiently valid for practical purposes.

It was recommended—again arbitrarily—that those with three or more minor defects and those with major defects be retired as unfit for patrol duty. Not much attention was paid to these recommendations, the mayor acting on his own

TABLE 1 *Physical Status of 230 Police Officers Five Years after Classification on the Basis of a Simple Physical Examination*

CLASSIFICATION	DEAD	PENSIONED OR DISCHARGED	ON ACTIVE DUTY
	%	%	%
Group A	1	5	94
Group B	4	3	93
Group C	12	12	76
Group D	20	45	35

discretion. Five years later I investigated the status of all 230 men, with the results shown in Table 1.

In view of the rough prognostic accuracy reflected in results such as these, it is quite reasonable to strive for a better estimate of physical fitness than that obtained from a mere certification of the absence of disease or the presence of minor or major physical abnormalities. Many attempts have been made to evaluate physical fitness. One of these, which may be taken as representative since it embodies both the virtues and the defects of several others, is the so-called Schneider index, which has been widely used in the examination of prospective aviators. This was devised in 1920 by Edward C. Schneider,¹ of the United States Air Service Medical Research Laboratory. The index is arrived at by grading on a scale of -3 to +3 the response of an individual to six observations, as follows:

Reclining pulse rate, for example, a rate of 101 to 110 receives a grade of -1, a rate of 50 to 60 a grade of +3.

Increase in pulse rate on rising from a reclining position, for example, an increase of 35 to 42 from a reclining rate of 81 to 110 receives a grade of -3, an increase of 0 to 10 from a reclining rate of 50 to 80 a grade of +3.

Standing pulse rate, for example, a rate of 131 to 140

receives a grade of -1, a rate of 60 to 70 a grade of +3.

Increase in pulse rate immediately after exercise, for example, an increase of 41 to 50 from a standing rate of 100 to 140 receives a grade of -3, an increase of 0 to 10 from a standing rate of 60 to 90 a grade of +3.

Return of pulse rate to standing normal after exercise, for example, a return to normal within 0 to 60 seconds receives a grade of +3, one within 90 to 120 seconds a grade of +1, and a return to a level of 11 to 30 above normal after 120 seconds a grade of -1.

Change in systolic blood pressure in the standing position as compared with the reclining position, for example, a rise of 8 mm. of mercury or more is given a grade of +3, a fall of 6 mm. or more a grade of -1.

A cumulative total score of 9 or less is said to indicate physical unfitness, whereas a score of 10 or more indicates physical fitness.

A diagnosis of physical fitness based on such a test as this may properly be questioned not only on the basis of the physiological validity of the required responses, but also in respect to the meaning of the term "physical fitness."

A proper test of physical fitness must take into consideration the varying capacities of men, women and children at different ages to withstand specified strains or to accomplish specified objectives. Observations such as those of Robinson,² indicating the variations at different ages in the heart rate, lung ventilation, lung volume, oxygen capacity of the blood, hyperglycemia after severe work and adjustment to work, are of fundamental importance in arranging tests of physical capacity.

The consideration, too, of personality differences in evaluating the results of quantitative tests is of decided significance. Thompson,³ at the Harvard University Fatigue Laboratory, has found, for example, that outstanding airplane pilots uniformly take in larger volumes of air during a normal inspiration—that is, they have a greater volume of tidal air—than a group of non fliers of corresponding health and physique, and is inclined to attribute this difference in physiological pattern to a difference in temperament. The knowledge we possess in regard to correlation between physiological and psychological or mental variations is limited, and the field although promising, is as yet largely unexplored.

When a sufficient amount of data of this sort is available, it may be possible to apply it in the construction of tests of physical fitness which will tell us not only whether an individual is physically fit as compared to others of his group, but, more significantly, what sort of activity he is best adapted to perform. Data already at hand enable us to understand how Clarence De Mar at the age of thirty-seven was able to outdistance his younger competitors in the Boston Athletic Association marathon run, and why short dashes

re more apt to be won by younger men than by older. What sort of test can be devised which will tell us how a psychoneurotic, physical runt like T. E. Lawrence, who would almost certainly have been rejected for military service by an ordinarily competent medical examiner could nevertheless, almost single-handedly accomplish the deeds recounted in *The Revolt in the Desert* and the establishment of the Kingdom of Iraq?

Until group examinations have attained a far higher degree of efficient selectivity than they now possess, a certain amount of injustice is likely to be involved in attempts to maintain rigid standards based on their results. It is of course necessary that personal rights and liberties be respected. Workmen have not infrequently objected to company insurance on the ground that routine medical examination of employees allows an employer to use so-called physical unfitness as an excuse for getting rid of unwanted employees in opposition to medical examinations of automobiles might be expected not only from rejected drivers but also from automobile dealers and accessory salesmen who might feel that their personal liberty had been infringed if many automobiles were ruled off the road because of physical or mental defects. This matter was well considered by John Stuart Mill⁴ who asserted: "Whenever there is a definite damage or a definite risk of damage, either to an individual or to the public, the case is taken out of the province of liberty and placed in that of morality or law." A survey of group examinations shows that the need for them has developed in four main fields: accident and health insurance, public services such as the Army and the Navy, police and fire departments, railways and air services, industrial medicine, and public health and preventive medicine.

INSURANCE EXAMINATIONS

The pioneer work in devising examinations adapted to the selection of good physical and mental risks was performed done by the life insurance companies. Many group-examination forms have been based on the medical forms used by these companies. They are chiefly interested in longevity and those factors which affect the expectation of life. The chief aims of their examinations appear to be as follows: to pick healthy people to attract people conforming to a standard type concerning which mortality figures or life-expectancy figures are available, to eliminate groups known to have a short life expectancy and to rule out people with certain specified diseases. The specialist in this branch of medicine can tell us whether the life insurance examination can be

simplified, improved or standardized on the basis of collected data. He can also supply us from his files with medical information of wide interest. We have all learned, for example, of the important correlation demonstrable between overweight and increased mortality from diabetes and circulatory disease. Other facts are available. The late Dr. Edwin W. Dwight, former medical director of the New England Life Insurance Company, once pointed out to me an interesting correlation between a family history of nervousness, nervous or mental disease, and death in middle age. Such a family history was of no significance in the case of the ordinary professional man, merchant, farmer or mechanic, but was associated with a sharp rise in death from accidental causes, for example suicide, during middle life when found in the family background of bankers, stockbrokers and others whose fortunes rose and fell with the stock market. In men likely to be subjected to sudden nervous strain due to financial crises, the family tendency to "nervousness," vague though this term may seem to be, was found to be of statistical significance to the company. It might also be of interest to the director of vocational guidance.

The type of selective examination best adapted to accident insurance and health insurance companies is different from that required by life insurance examiners. Data acquired by experience in this field may well be of concern to those who envision a wider application of the principle of health insurance through private or governmental agencies.

PUBLIC SERVICES

The leading public services, the Army and the Navy, police and fire departments, air transport companies and railways, all have group examination procedures of their own which are in constant process of development and improvement. The necessity for such special types is obvious.

The Army and the Navy not only exercise rigid selection in assigning men for training or service, but also provide for periodic re-examination. This insistence on maintenance of physical and mental efficiency is not apparent elsewhere. Practically all our municipalities require a rigid physical examination of candidates for the police and fire departments, but few if any attempt to maintain physical standards, by means of subsequent periodic re-examination, after membership in the force has been attained.

Medicine as applied to aviation presents many problems. Among these are the effect of high altitudes on normal persons, those with circulatory impairments, nervous invalids and others. The selection of candidates for training, either military or civilian, and the protection of the lives

of aviators and their passengers. The only persons likely to be examined in groups in this connection are student aviators and licensed pilots. The examination of the former is aimed at the selection of men who will make the best aviators, that of licensed pilots is intended to minimize accidents, and to weed out those who by reason of age, disability or infirmity are no longer fit for their duties.

As is well known, the physical and mental qualifications of candidates for aviation service in the Army and the Navy are extremely high, and a great deal of study has been given to the matter of qualification for the various classifications of fliers. In the military branch, opportunity has been freely afforded for investigative work aimed at improving formal standards, and some tests, such as the complex co-ordination tests, have reached a high degree of development and application, even though they are not as yet obligatory. Dr L. J. O'Rourke⁵ is a pioneer in this field, and gives the following illustration of the great possibilities of such tests:

Lieutenant K. reported for tests. K. was possibly the best liked man on the post, calm, a perfect physical specimen, [and] seemed to be the most even tempered man on the post. He secured a AA on all his ratings, which were done by one or two out of five or ten thousand. While playing with the reaction time material I threw on a double reaction and a confusion [that is a buzzer intended to distract the subject during his reaction period]. He seemed to be so absolutely perfect that I wanted to see what he would do. Immediately he stopped and did nothing. I tried it seven times during that run, and each time when he got the double confusion his reaction time slowed and in each case he failed to do anything. I rated him as dangerous and I became very unpopular on the post.

All our other tests showed him to be a AA man. After considerable discussion he was permitted to go on. As the War Department records will show, on his first solo flight he killed himself—due to an unusual problem that came up in air or wind and he was unable to co-ordinate. His reaction time was slow and he crashed.

INDUSTRIAL MEDICINE

Industrial organizations often require the physical examination of applicants for employment or of candidates for promotion. This may legitimately be done for the purpose of determining the aptitude of the prospective employee for the work to which he may be assigned, or to secure as healthy workers as possible in order that the economic loss from absences due to illness may be minimized, or to reduce the employer's chances of assuming liability in case of illness or accident while at work. Standard insurance forms may be adequate for some of these purposes, but they will hardly serve as aptitude tests, or for selecting the

best candidates, other qualifications being assumed, for promotion. Each industry has its own specific problems, and no blanket form can serve them all. A telephone company employing large numbers of young women as switchboard operators may find that the prevention of psychoneuroses or of dysmenorrhea is especially important, while a manufacturer of explosives may find that employees with normal vascular systems are resistant to chronic nitrite poisoning, and center his attention there. The special problems of industrial medicine are beyond the scope of this paper, suffice it to say that group examinations of specialized type are a necessary part of the program.

The need of fitting the examination to its purpose is here again to be emphasized. To do this requires close consideration of the end in view by those who plan the group examination. To reject a candidate for life insurance or charge him a high premium because of a systolic murmur or an inguinal hernia may be quite proper and in accordance with the experience of insurance companies, but to discharge a skilled designer of fabrics from a job he has held for many years in a textile mill because of these impairments, as was done in one case that came to my attention, seems absurd and unjust.

The problem is not only one for the employer and employee. It has its public interest, especially in the field of vocational guidance. This, like many other new fields, has not been overlooked by the quack with a formula. Vocational aptitude tests based perhaps on vocabulary and selling for twenty-five dollars, even though promulgated by psychologists and widely sold to the public, require impartial analysis by unbiased investigators before being accepted as authoritative.

PUBLIC HEALTH AND PREVENTIVE MEDICINE

Finally, the group examination is of increasing significance in the field of public health and preventive medicine. Here the so-called periodic health examination comes in for attention. Much space could be devoted to a discussion of the practicability and desirability of the routine examination of healthy persons, and of the results reasonably to be expected therefrom. Surely no one type of health examination can be devised which will properly evaluate the health hazards of any individual. The dangers confronting the infant and child are not identical with those faced by the middle-aged. Whether tuberculosis examinations, cancer examinations or cardiac examinations should be advocated instead of "health" examinations is a matter for consideration.

At any rate, it is possible to foresee the types of routine physical examinations likely to be de-

veloped to a point of greater efficiency. Such are examinations of the baby and the pre school child, of public-school pupils and of college students, groups each of which has its own health hazards and therefore requires a different emphasis in routine inspection.

Premarital examinations are being widely urged. Will a positive Wassermann test forever bar an otherwise healthy young man from marrying? It could apparently do so if we took seriously—as our legislatures may at any time decide to do if not advised against it—the well meant agitation of various groups interested in social betterment. There are many conditions, such as insanity, feeble-mindedness, active or communicable tuberculosis and gonorrhea or syphilis, which might make marriage unsafe or improper. The establishment of proper standards and the arrangement of suitable types of examination to discover these impediments to marriage surely deserve the careful attention of the medical profession.

We are or may be called on to furnish certificates of medical fitness for barbers, servers of food and nursemaids. In some realistic countries the campaign against venereal disease includes routine examinations of prostitutes. Eugenic programs, sterilization projects and the examination of defectives and prison inmates offer other fields for consideration. The collection of data, the standardization of procedures and the methods of examination must be determined with the cooperation of the best expert medical opinion that can be supplied.

The examination of applicants for licenses to operate motor vehicles has attracted the attention of a number of influential groups. Its purposes are to safeguard the driver himself against accident, to protect pedestrians and drivers of other vehicles and to help reduce the economic loss due to accidents. Should the emphasis be placed on requirements for good vision on the absence of physical impairments, on character or personality traits, or on routine inspections for alcoholism among drivers on the highways?

There is little question that drivers who are physically and mentally normal are less frequently involved in accidents than are abnormal persons. Data are available in regard to the effect of the ingestion of alcohol. Holcomb⁶ found by

means of routine examinations for the presence of alcohol in the blood, that in a group of drivers in accidents causing personal injury there were thirty three times as many whose blood contained 1.5 parts per thousand (regarded as conclusive evidence of being under the influence of alcohol) as there were in the general driving population. Twelve per cent of drivers on the highways of Illinois had been drinking. Among drivers involved in accidents, however 47 per cent had been drinking.

Periodic inspection might determine not only the state of alcohol saturation of the driving public, but such matters as intact motor function, mental condition, use of the extremities, vision (simple and color) and hearing and reaction times.

Twenty five states now include a check of vision as part of their drivers examination. The National Safety Council has issued pamphlets presenting what are regarded as the best present and most desirable future practices in examining drivers. Medical examinations are obligatory for all drivers of automobiles in Germany, Bulgaria, Denmark, Holland, Hungary, Italy, Luxembourg, Norway, Sweden and Yugoslavia, with varying provisions for re-examination at intervals of one to six years depending on the age of the driver.⁷

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These matters are of growing importance. As physicians we are being called on more and more often to conduct any or all these types of group examinations or to give advice as to their administration. We must prepare ourselves to do so in the same spirit and with the same systematic caution that we employ in the practice of diagnostic and therapeutic medicine, and we must combat quackery in group examinations just as alertly as in other fields of practice.

5 Bay State Road.

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DRUG THERAPY IN CASES OF INFANTILE CEREBRAL PALSY AND ALLIED DISORDERS, WITH SPECIAL REFERENCE TO HYOSCINE*

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A CONSIDERABLE body of literature has grown up concerning the etiology, diagnosis and treatment of infantile cerebral palsies. Heyman¹ in a recent article pointed out the multiplicity of causes. Phelps² and others have written comprehensively on diagnosis and treatment. Individual variations are striking, but the picture usually contains one or more of the following classic features: spasticity, tremor, inco-ordination, choreiform and athetoid movements and mental deficiency. The last-named defect is very difficult to evaluate because of the associated physical handicaps, but should be determined early because of the prolonged, arduous nature of the treatment and the need for compensatory intellectual assets.

As Phelps³ has emphasized, "The training of such children is a general problem and involves the orthopedic, psychologic, speech and educational fields." These headings include hydrotherapy, massage and active and passive exercises. Such a program is being carried out on a selected group of patients at the Emma Pendleton Bradley Home, an institution devoted to the treatment of the neurologic and behavior disorders of childhood. It should be noted that the training described above includes no assistance from drug therapy. A search of the literature reveals no article describing a pharmacologic approach to these cases. In considering the problem the hypothesis was entertained that treatment of these children with a drug in the atropine group might reduce the hypertonus, influence the athetosis, speed up the process of the training and eliminate the annoying drooling. Attention was therefore directed toward this group.

Toward the close of the nineteenth century Erb⁴ found that hyoscine (scopolamine) was much more effective in controlling the tremor and relieving the rigidity in parkinsonism than was any remedy previously employed. In physiological experiments on spasticity Walshe⁵ found that the rigidity of the hemiplegic type of spastic paralysis and that of paralysis agitans are similar in nature and depend on the proprioceptive reflex from the

muscle. This point gains further support from the experimental work of Davis and Pollock,⁶ muscle tonus. We should therefore be able to influence this symptom by the use of atropine or an allied preparation. The drug of choice is hyoscine hydrobromide because of its widespread use in the parkinsonian syndrome. It was started in June, 1936, on a group of 6 cases and was continued, with minor interruptions, over a period of two and a half years. All these cases were carefully worked up and the patients had been in the hospital for a sufficient period of time for a baseline to be established against which to evaluate changes occurring during the clinical investigations. There was no change in the treatment program other than the addition of the drug therapy. During the course of this study the hyoscine was discontinued and the effects of three other drugs—phenobarbital, amphetamine (Benzedrine) and atropine, were tested over two week periods. All these drugs were given by mouth. The effect of withdrawal of hyoscine and the tolerance that might be developed were also noted. The results of the drug therapy were evaluated by combining the independent observations of trained workers,—physiotherapists, teachers and nurses,—the reports of examining physicians and the study of moving pictures which were taken from time to time.

The following condensed reports indicate type, duration and results of the drug therapy.

CASE 1. N. B., a 5 year-old boy, was admitted February 4, 1936. The family history was negative except for a similar difficulty which had developed in a young sibling. The birth history was normal. Onset with tremor began at the age of 6 months, with increasing disability. At the time of admission the patient was unable to walk and showed marked generalized tremors, spasticity and drooling. Routine therapy for 4 months resulted in practically no improvement. On hyoscine hydrobromide, 1/100 gr. three times daily, he learned to walk in 3 days, drooling and involuntary movements were greatly reduced and speech was improved. After 10 days on hyoscine the drug was withdrawn, whereupon the patient rapidly slipped back to his former state and was no longer able to walk. After 1 week without medication hyoscine was resumed, with a rapid return of the improvement previously noted. Because of some restlessness and difficulty in sleeping the dose was changed to 1/200 gr. twice daily which maintained the improvement without any untoward

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§For convenience ages are given as of the time of starting drug therapy.

side effects. After 9 months on hyoscine it was again discontinued. Although the patient had been receiving this drug for a long period of time and it had been stopped suddenly there were no mental disturbances. The drooling and tremors quickly returned and although there was some improvement within a few weeks, he had still not returned to his former level after 6 weeks. Immediate improvement was again noted when the hyoscine medication was recommenced. After 2 years some slowing up in progress was noted, but was checked effectively by increasing the dose to 1/200 gr three times daily. On phenobarbital, 1/2 gr three times a day the patient was sluggish and the tremors were more marked. On amphetamine sulfate, 10 mg. daily he was tense and irritable. On atropine sulfate, 1/200 gr twice daily the tremors were diminished, but not to the same extent as with the hyoscine and the general behavior was at a lower level. It should be noted that for the first 6 months of his life this child was considered normal and that there was definite progression in his disability during the next 12 months; therefore his condition probably represents a different clinical entity from the so-called cerebral palsy but for practical classification as to care and treatment he fitted in easily with the above-mentioned group.

CASE 2. W. M., a 9-year-old boy was admitted June 12, 1931. The family history was negative except for diabetes in the mother, which complicated the pregnancy. The birth was a full-term, instrumental delivery. Laid asphyxia was present, and only after a considerable period of mouth-to-mouth insufflation were respirations established. When the apyrexial coma had passed it was noted that he held his extremities in spastic attitudes. His development was very retarded. It was not until he was 7 years of age that he began to take a few steps. His progress during the next 2 years was extremely slow. His walking was interfered with by an extreme degree of spasticity and by wild bursts of choreoathetoid movements. Drooling was an outstanding symptom. When treatment was started he could get about with the aid of canes, but his progression was painfully slow. He was started on hyoscine 1/200 gr three times daily but this was soon dropped to twice daily because of flushing and slight rise of temperature. He was lethargic at first, but in spite of this, walking promptly improved. Drooling was immediately stopped by hyoscine. During a brief period when he was off the medication the drooling returned and athetosis again began to interfere with walking. When hyoscine was recommenced there was an immediate improvement in co-ordination. There was a noticeable improvement in posture and stride, better relaxation, increased confidence and a diminution of athetoid movements. In all he patient was observed over a 9-month period with this medication. Occasionally dryness of the mouth and flushing were noted but the dose was not decreased again because of these symptoms. On withdrawal there were no mental disturbances other than a lessening of confidence and initiative. There was an immediate increase in over-lower movements, but the patient gained considerable control over these within the next 10 days. On phenobarbital 1/2 gr three times daily he began to manifest more athetosis. On amphetamine sulfate, 10 mg., there was less nervousness and he walked better but he was tense and less able to concentrate. Atropine sulfate, 1/200 gr twice daily produced essentially the same effect on the neuromuscular system as had hyoscine but there was not the same increase in confidence and initiative.

CASE 3. F. F., a 4-year-old boy was admitted May 21, 1932. The family history was negative. The mother's pregnancy was complicated by severe hypertension. The birth itself was considered normal. At the time of admission at about 2 years of age, he was unable to walk or even sit alone. Physical examination showed the arms to be weak and poorly co-ordinated. The legs were spastic and attempts to walk with support showed a typical scissors gait. During the next 2 years in the hospital he made very slow but steady progress so that he learned to sit and stand alone. He was given daily physiotherapy. During April and the greater part of May 1936, he was absent from the hospital and received no physiotherapy until June 1. On June 19 he was started on hyoscine, 1/200 gr three times daily which was dropped to twice daily 2 days later on account of restlessness and insomnia. On medication the drooling stopped and the muscular co-ordination immediately improved, so that 11 days later the patient was ahead, in his muscular skill, of the point he had reached at the time he left the hospital. There was also an immediate improvement in speech. After 9 months without increase in dosage the medication was stopped. Drooling reappeared and inco-ordination was much more apparent. There was a slight falling off in skill but recovery within a few weeks to the level which had obtained prior to the use of drug therapy since progress was slowed the patient was put back on hyoscine. On phenobarbital 1/2 gr three times daily he was retarded and irritable. On 10 mg. of amphetamine sulfate he was restless and tense. On atropine sulfate, 1/200 gr twice daily the same physical improvement was noted as with hyoscine, but the patient was much more irritable.

CASE 4. M. M., a 4-year-old boy was admitted August 20, 1935. The family history was negative. The mother's pregnancy with this child was complicated by edema and convulsions. Labor was induced in the 7th month. The birth weight was 3 pounds 4 ounces. At the time of admission the child could not walk or sit unaided. Physical examination revealed a typical quadriplegia with considerable spasticity, especially in the legs. Progress in motor skill in spite of daily physiotherapy was very poor. On June 18, 1936 the patient was started on hyoscine, 1/200 gr three times daily. The dose was reduced markedly and finally discontinued because of sleeplessness and enuresis. However, the patient later showed similar symptoms when not on medication. Under the hyoscine there was relief from drooling and a questionable improvement in relaxation. On phenobarbital 1/2 gr three times daily there was better relaxation but general progress was retarded. On amphetamine sulfate the patient was much more tense. On atropine sulfate he reacted poorly becoming more tense and excited and less free in his movements.

CASE 5. J. G., a 5-year-old Negro boy was admitted August 6, 1935. The family history was negative. The pregnancy had terminated spontaneously in the 7th month. The child gained very slowly during the first few months, and a marked spasticity especially of the lower limbs, was noted from an early age. At the time of admission he was unable to walk owing to the spasticity but by the time drug therapy was started he was able to get about with the aid of canes. Drooling was prominent. The patient was started on hyoscine hydrobromide, 1/200 gr three times daily. Under this medication he was more active and more confident with somewhat better relaxation but showed no improvement in spasticity. On withdrawal of the hyoscine, drooling returned and he was less

agreeable. On Luminal he was more relaxed but showed retardation. On amphetamine sulfate he was more alert but relaxation was poor. He received atropine sulfate, 1/200 gr twice daily, for 8 days, with very little change.

CASE 6 C F, a 14-year-old boy, was admitted June 14, 1939. The family history was not unusual. The birth was difficult. Lived asphyxiated was present in the infant, and it was some time before normal spontaneous respirations were established. Marked spasticity and choreo-athetosis were noted from an early age. Speech was developed early but was very dysarthric. Intelligence was at a superior level. Under long-continued physiotherapy the patient learned to walk, but his progress was painfully slow and he never developed a good posture. Walking was often interrupted by bursts of severe choreoathetosis. Drooling was present. He was started on hyoscine hydrobromide, 1/200 gr three times daily. This dose was slowly increased to 1/50 gr three times daily, which was maintained 1 week, but since there was no more change in physical progress and no correlated change, the medication was stopped without any change in attitude or behavior. Hyoscine was considered to have been ineffective in this case except for the control of drooling.

Under hyoscine therapy, drooling was abolished in all cases. Offhand this may seem to be of little consequence, but practically it looms rather large in the management of these patients. If salivation is excessive their belongings and clothing are constantly moist and it proves very difficult to keep the children dry and warm out-of-doors in the wintertime. In 5 of the 6 cases reported increased confidence was noted. This may have been due to the central action of the drug or to the encouragement of more rapid progress and better control of muscular activity. Three of the 6 patients exhibited increased relaxation and lessening of involuntary muscular movements and improvement was obvious. In 2 of these cases the gain was definite but not particularly dramatic, but in the third (Case 1) it was striking, since the child learned to walk again in three days. It is true that the gain in some of the cases was small, but when one considers what difficult problems these are, the slight effort and expense entailed in providing them with this medication are well worth while. It should be noted that the beneficial result appears early if at all, so that a long period of trial is unnecessary.

No contraindications to hyoscine therapy were established. One child reacted poorly when hyoscine was instituted but later had similar reactions when not on medication. The effective dose produced no disturbing or distressing side effects. There was no evidence of increasing tolerance. The dose in one case was increased after two years, but the child had of course gained in weight and stature during that period. The question of addiction has been considered. The only report found on this is by Schiltensbrand,⁷ who observed a rapid deterioration in the condition of patients

with postencephalitic parkinsonism when hyoscine was discontinued. This does not coincide with the views of many clinicians, nor was such a change observed in our series. As indicated in the case reports, the treatment was suddenly discontinued after the children had been kept on the medication for many months. There usually followed a period during which the child's motor performance was definitely inferior to what it had been while on drug therapy, but in no case was he any worse than when the treatment was instituted, and after a short period of readjustment the patient returned to a state superior to that observed at the time medication was begun.

The reaction to the other drugs employed was disappointing. The responses to phenobarbital, amphetamine sulfate and atropine sulfate were successively investigated. This was done by cutting all previous medication, establishing a new baseline and evaluating the response to the new drug by co-ordinating the reports of various observers. Five patients in this group received phenobarbital, 1/2 gr three times daily. All seemed to be retarded, one showed considerable irritability, and another exhibited increased athetoid movements. On 10 mg of amphetamine sulfate daily 5 children were tense and irritable and could not relax. Five children received atropine sulfate, 1/200 gr twice daily, by mouth. Excessive drooling was stopped in all cases. Two children showed decrease in the athetosis, but they did not have the same confidence as they had had while on hyoscine. Two patients became tense and excited. The fifth child showed little change.

CONCLUSIONS

The present therapeutic approach to the problem of the spastic child takes advantage of many forms of therapy, but it is believed that drug therapy has not received adequate trial.

A few carefully studied cases were placed on hyoscine hydrobromide. The usual maintenance dose was 1/200 gr given twice daily by mouth. The response was most encouraging in that drooling was stopped, athetosis lessened, confidence increased, relaxation improved and progress in retraining more rapid. One child learned to walk in three days.

No general contraindications to hyoscine were established. In particular, there was no increasing tolerance, no annoying side effects, and no untoward symptoms even when the drug was suddenly withdrawn after periods as long as nine months.

The favorable response to hyoscine came early or not at all. Amphetamine (Benzedrine) sulfate, phenobar-

bitol and atropine sulfate were investigated clinically in the same series. The therapeutic results of this part of the study were disappointing.

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A COMPARISON OF THE DAVIES-HINTON AND WASSERMANN REACTIONS IN THE CEREBROSPINAL FLUID

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THE Hinton flocculation test for syphilis has been modified by Davies¹ to make it applicable to the cerebrospinal fluid. Since 1936 the Massachusetts State Wassermann Laboratory† has been routinely testing all samples of cerebrospinal fluid by this method, provided there was sufficient fluid remaining after the Wassermann test had been performed. The present study is based on the results of 2110 consecutive simultaneous Davies-Hinton and Wassermann tests done at the Wassermann Laboratory on the cerebrospinal fluids of patients in the Boston City Hospital from 1936 to 1938.

There was agreement between the two tests on 2052 occasions (97.2 per cent) and disagreement on 58 (2.8 per cent), as shown in Table 1. The

test was positive in every fluid in which the Wassermann reaction was positive. Disagreement between the two tests occurred only in those fluids in which the Wassermann reaction was doubtful or negative. The Davies-Hinton test was positive in 51 fluids in which the Wassermann test was

TABLE 2. Analysis of the Disagreements between the Davies-Hinton and Wassermann Reactions on the Cerebrospinal Fluid of 50 Patients

RESULTS	NO. TESTS OF FLUID	TREATED FOR LATENT OR SYSTEMIC SYPHILIS	TREATED FOR NEURO- SYPHILIS
Davies-Hinton positive Wassermann negative	9*	9	10
Davies-Hinton positive Wassermann doubtful	2†	3	11
Davies-Hinton doubtful Wassermann negative	2	1	2
Davies-Hinton negative Wassermann doubtful	0	1	0
Totals	13	14	23

*Davies-Hinton positive and Wassermann doubtful in three subsequent fluids from 1 of these patients.

†Two subsequent examinations of the fluid in 1 patient resulted in one positive and one negative Davies-Hinton and two doubtful Wassermann reactions.

TABLE 1. Comparison of Davies-Hinton and Wassermann Tests on 2110 Cerebrospinal Fluids

RESULTS	NO. OF FLUIDS
Both tests negative	1896
Both tests positive	152
Both tests doubtful	4
Total agreements	2052
Davies-Hinton positive Wassermann negative	30
Davies-Hinton positive Wassermann doubtful	21
Davies-Hinton doubtful Wassermann negative	5
Davies-Hinton negative Wassermann doubtful	2
Total disagreements	58

Wassermann reaction was positive in 152 fluids, doubtful—that is positive only in 2 cc. of the fluid—in 27 and negative in 1931. On these same fluids the Davies-Hinton test was positive in 203, doubtful in 9 and negative in 1898. The Davies-Hinton

negative (30 fluids) or doubtful (21 fluids) in addition the Davies-Hinton test was doubtful in 5 fluids which gave a negative Wassermann reaction while there were only 2 fluids with a doubtful Wassermann and a negative Davies-Hinton reaction.

It is clear that in assessing the relative value of the two tests a careful analysis of these 58 disagreements is essential. It was found that the 58 specimens came from 50 different patients, whose records were therefore carefully reviewed (Table 2). These patients fell into three main groups: those with no known history of having received antisyphilitic treatment (13 patients), those who had been treated for primary, secondary, tertiary or latent syphilis with no clinical evidence of involvement of the central nervous system (14 patients) and those who had been treated for syph

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The authors are indebted to Dr. W. A. Hinton, director of the Massachusetts State Wassermann Laboratory for report of the results on 11 of the fluids from the Boston City Hospital.

ilis of the central nervous system (23 patients). Since 37 of these 50 patients had received antisyphilitic treatment and since at least 1500, and probably nearer 1700, of the entire series of tests were in apparently nonsyphilitic subjects, it is at once clear that disagreements occurred more than ten times as often in patients under treatment as in the remainder of the group. But a consideration of Table 3 yields an even more striking result.

TABLE 3 *Disagreement between the Davies-Hinton and Wassermann Reactions on the Cerebrospinal Fluid of 13 Patients with No History of Treatment for Syphilis*

CASE NO.	DAVIES-HINTON REACTION	WASSERMANN REACTION	SPINAL-FLUID PROTEIN mg / 100 cc	SERUM HINTON REACTION	DIAGNOSIS
1	Positive	Negative	618	Unknown	Cerebellar hemorrhage
2	Positive	Negative	103	Positive	Subdural hematoma
3	Positive	Negative	70	Positive	Brain tumor (verified)
4	Positive	Doubtful	Not done	Positive	Meningococcal meningitis
5	Positive	Positive	2400	Unknown	Cerebral hemorrhage
6	Doubtful	Negative	47	Positive	Carcinoma of lip with metastases
7	Positive	Negative	103	Positive	Tabes dorsalis
8	Not done	Positive	16	Unknown	Alcoholism terminal bronchopneumonia
9	Positive	Negative	31	Positive	Latent syphilis
10	Positive	Negative	Not done	Positive	Brain tumor suspect
				Negative	possible syphilis of the central nervous system
				Doubtful	
11	Doubtful	Negative	22	Positive	Serological syphilis
12	Positive	Doubtful	22	Doubtful	pyelitis
	Positive	Doubtful	25	Positive	Tabes dorsalis
	Positive	Doubtful			
	Positive	Negative			
13	Positive	Doubtful	29	Positive	Tabes dorsalis
	Positive	Doubtful	33		
	Negative	Doubtful			
	Not done	Doubtful			
	Not done	Positive			

All except 3 of the 13 patients with no history of previous antisyphilitic treatment had either consistently or on occasion a positive blood Hinton test. In the exceptions the patients had died before blood for a serological test was taken. Hence if we cannot say that all the disagreements occurred in syphilitic patients, we can at least say that no disagreement occurred in a proved nonsyphilitic patient.

Disagreement of the Tests in Patients with No Previous Antisyphilitic Therapy

The first 5 of the patients in Table 3 (no history of antisyphilitic treatment) had an excess of protein in the cerebrospinal fluid which could be attributed to factors other than syphilis. It is possible that the positive (in 1 case doubtful) Davies-Hinton reaction in the cerebrospinal fluid was due to the presence of serum protein which contained syphilitic reagin. The fluid was frank-

ly bloody in 2 patients owing to cerebral hemorrhage, 1 patient had meningococcal meningitis, 1 a brain tumor, and 1 a subdural hematoma.

Three of the 8 remaining cases with no history of treatment (Table 3) showed clinical evidence of syphilis of the central nervous system (tabes dorsalis). In these 3 cases, the Davies-Hinton reaction was a more reliable aid in diagnosis than the Wassermann reaction, though in 1 case even the Davies-Hinton was negative on one occasion, and in 2 of the 3 cases a positive Wassermann reaction was finally obtained. In the remaining 5 cases in this group there was no clinical or serological evidence in favor of syphilis of the central nervous system except the Davies-Hinton reaction, which was positive in 4 cases and questionable in 1.

To sum up, there was disagreement in 5 patients with no history of antisyphilitic treatment whose fluids were contaminated with serum protein which possibly contained syphilitic reagin. In the 8 remaining patients (13 fluids) the Davies-Hinton reaction was thrice positive and once doubtful in patients with no other evidence of syphilis of the central nervous system, once positive in a patient in whom this diagnosis was doubtful, and once negative in a patient with tabes dorsalis. In the same 8 patients (16 fluids) the Wassermann reaction was twice negative and seven times doubtful in the 3 patients with tabes dorsalis. The most

TABLE 4 *Disagreement between the Davies-Hinton and Wassermann Reactions on the Cerebrospinal Fluids of 14 Patients with Positive Blood Hinton Tests Who Were Receiving Treatment for Syphilis but Who Had No Clinical Evidence of Syphilis of the Central Nervous System*

CASE NO.	DAVIES-HINTON REACTION	WASSERMANN REACTION	SPINAL FLUID PROTEIN mg per 100 cc	DURATION OF TREATMENT
14	Positive	Negative	25	5 yr *
15	Positive	Negative	25	1 yr
16	Positive	Negative	30	4 yr
17	Positive	Negative	36	2 yr
18	Positive	Negative	76	2 yr †
19	Positive	Negative	27	2 yr
20	Positive	Negative	40	†
21	Positive	Negative	51	§
22	Positive	Negative	34	1 mo
23	Positive	Negative	70	2 yr
24	Positive	Doubtful	21	2 yr
25	Positive	Doubtful	28	2½ yr †
26	Doubtful	Negative	27	2 yr
27	Negative	Doubtful	25	4 yr

*Patient had left pyramidal tract signs.

†Bloody tap 41 500 red blood cells per cubic millimeter in spinal fluid.

‡No recent treatment but considerable treatment in past years.

§No recent treatment but considerable treatment in past years signs of diffuse encephalomalacia blood pressure 150/90

¶Mid zone gold sol curve

striking difference between the two tests, therefore, is that the Wassermann reaction was never positive or doubtful in any of the patients without other evidences of syphilis of the central nervous system, although it was often doubtful or negative in patients with such evidence, while the Davies-Hinton

action was only once negative in a patient with her evidence of syphilis of the central nervous system, although it was several times positive or doubtful in patients without such evidence.

Disagreement of the Tests in Patients Receiving Treatment for Syphilis Other Than Neurosyphilis

Turning now to the 14 patients (Table 4) who had received or were receiving treatment for syphilitic syphilis we note that in 1 of them (Case 18) the positive Davies-Hinton reaction was possibly due to the presence of blood containing syphilitic antigen in the cerebrospinal fluid resulting from a bloody tap. Of the 13 other cases, 3 with a positive Davies-Hinton reaction had an increased spinal fluid protein or abnormal colloidal gold reaction. The Wassermann reaction was negative in one and questionable in two of these three fluids. This leaves 10 cases without supporting evidence of neurosyphilis, in which the Davies-Hinton reaction was positive in 8, questionable in 1 and negative in 1, while the Wassermann reaction was negative in 8 and questionable in 2. It should be mentioned here that in the 1 case in which the Davies-Hinton reaction was negative and the Wassermann reaction questionable, a subsequent lumbar puncture eight months later showed a negative Wassermann reaction.

Disagreement of the Tests in Patients under Treatment for Syphilis of the Central Nervous System

The final group of patients (Table 5) is composed of those who had received or were receiving treatment for known syphilis of the central nervous system. A comparison of the two serological reactions here yields results quite comparable to those found in the previous groups. Of the 10 cases in which the Davies-Hinton was positive and the Wassermann reaction negative 3 showed other signs of continued activity of the syphilitic process. Of the 11 cases with the Davies-Hinton reaction positive and the Wassermann reaction doubtful, 4 showed other signs of activity. Neither of the 2 patients with questionable Davies-Hinton and negative Wassermann reactions had any other evidence of activity of the infection. Thus there were no cases with other signs of activity in which the Davies-Hinton reaction was negative, but 14 cases with positive Davies-Hinton reactions as well as 2 in which the reaction was doubtful had no other signs of activity. On the other hand the Wassermann reaction was negative in 3 and questionable in 4 cases in which there were other signs of continued activity, even though it was never positive in a case in which there were no other signs of activity.

DISCUSSION

Let us now consider what light this material throws on the relative value of the Wassermann and Davies-Hinton reactions in the cerebrospinal fluid, first diagnostically, and second as criteria of therapeutic progress or success.

In order to make the diagnosis of syphilis of the central nervous system, one has to answer affirmatively two questions: Has the patient syphilis? Is there sufficient evidence that the disease has involved the central nervous system? In most

Table 5. *Disagreement between the Davies-Hinton and Wassermann Tests on the Cerebrospinal Fluids of 23 Patients Receiving Treatment for Syphilis of the Central Nervous System*

NO.	DAVIES-HINTON REACTION	WASSERMANN REACTION	DIAGNOSIS	NUMBER OF YEARS SINCE TREATMENT	OTHER SIGNS OF ACTIVITY OF NEUROSYPHILIS
28	Positive	Negative	Vascular neurosyphilis	3	Increased protein in fluid
29	Positive	Negative	Tabs dorsalis	1	None
30	Positive	Negative	Tabs dorsalis	2	None
31	Positive	Negative	Tabs dorsalis	3	None
32	Positive	Negative	Asymptomatic neurosyphilis*	2	None
33	Positive	Negative	Tabs dorsalis	4	Lightning pains
34	Positive	Negative	Dementia paralytica	2	Increased protein in fluid
35	Positive	Negative	Vascular neurosyphilis	2	None
36	Positive	Negative	Tabs dorsalis	1	None
37	Positive	Negative	Tabs dorsalis; optic atrophy	2	None
38	Positive	Doubtful	Dementia paralytica	3	First zone gold-sol curve
39	Positive	Doubtful	Tabs dorsalis	1	None
40	Positive	Doubtful	Tabs dorsalis	1	None
41	Positive	Doubtful	Tabs dorsalis	2	Increased protein in fluid
42	Positive	Doubtful	Asymptomatic neurosyphilis	1	First zone gold-sol curve
43	Positive	Doubtful	Tabs dorsalis	3	None
44	Positive	Doubtful	Dementia paralytica	1	None
45	Positive	Doubtful	Dementia paralytica	2 1/2	None
46	Positive	Doubtful	Dementia paralytica	3	First zone gold-sol curve
47	Positive	Doubtful	Tabs dorsalis	1	None
48	Positive	Doubtful	Asymptomatic neurosyphilis*	1	None
49	Doubtful	Negative	Tabs dorsalis	3	None
50	Doubtful	Negative	Tabs dorsalis	2	None

*Diagnosis based on abnormalities found in specimen of cerebrospinal fluid removed six months to several years previously.

cases, of course, the answer to these questions is relatively simple. Occasionally it may be most difficult or even controversial.

In the 50 cases under consideration in which there was a disagreement between the Davies-Hinton and Wassermann reactions on the cerebrospinal fluid the diagnosis of syphilis of the central nervous system had been previously established in 23. If in addition we exclude the 6 cases in which the positive cerebrospinal fluid test was presumably due to the fortuitous presence of blood protein (with positive serum tests) in the cerebrospinal fluid, we have left 21 cases (27 tests)

in which there was a diagnostic problem. The answer to the first of the two questions we have to ask is relatively simple. Thirteen of the patients were treated syphilitics, 7 others were diagnosed as having syphilis on the basis of blood tests obtained at the time of the lumbar puncture in question and in the remaining patient no blood test was obtained. We may say, then, that in none of these cases in which information was available were there positive or questionable spinal-fluid Wassermann or Davies-Hinton reactions in the absence of systemic syphilis.

We now come to the question of the relative reliability of the two tests in indicating the presence or absence of involvement of the central nervous system. Heretofore it has been assumed that the presence of even a doubtful Wassermann reaction in an otherwise normal cerebrospinal fluid from a patient with syphilis but with no signs or symptoms of syphilis of the central nervous system was sufficient for the diagnosis of asymptomatic neurosyphilis. The question is now added: Does the occurrence of a positive or doubtful Davies-Hinton reaction under these circumstances have the same diagnostic importance? Unfortunately this cannot be answered as yet.

Turning to the relative value of the two reactions as therapeutic criteria, we see that in each of the cases in Table 5, all of which had at some time previously shown a positive Wassermann reaction in the cerebrospinal fluid, the Wassermann reaction under treatment became negative or doubtful while the Davies-Hinton reaction remained positive, or, as in the last 2 cases in the group, lagged behind the Wassermann reaction in the transition to negativity. Pursuing the problem somewhat further and more rigorously, we find that in the entire series of 2110 tests the spinal fluid Wassermann reaction had become negative in 41 of the approximately 200 patients who were under treatment for syphilis of the central nervous system. In these cases the Davies-Hinton reaction was negative in 29, doubtful in 2 and positive in 10. In other words, in nearly one third of all the cases in which the spinal-fluid Wassermann reaction had become negative, the Davies-Hinton was known to have lagged behind the Wassermann reaction in the transition to negativity.

It would appear, then, that in the treatment of syphilis of the central nervous system the Davies-

Hinton reaction tends to become negative either simultaneously with or subsequently to the Wassermann reaction. The question naturally arises, if the latter is the case, whether treatment should be continued until the Davies-Hinton reaction also becomes negative. One can only say at present that sufficient data are not available to enable one to answer this problem definitely. However, it is of interest to note that 4 of the cases with other signs of activity had a doubtful Wassermann reaction and 3 actually had a negative Wassermann reaction. The Davies-Hinton reaction, on the other hand, was invariably positive in this group when other signs of activity were present.*

SUMMARY AND CONCLUSIONS

Of 2110 consecutive, simultaneous Davies-Hinton and Wassermann reactions on the cerebrospinal fluid there was agreement in the results of the tests in 97.2 per cent and disagreement in 2.8 per cent.

Fluids with a positive Wassermann reaction always showed a positive Davies-Hinton reaction. In all but 2 of the cases of disagreement the Davies-Hinton was more positive than the Wassermann reaction.

No disagreements were found in nonsyphilitic patients.

A positive Davies-Hinton reaction was often found in syphilitic patients under treatment with no other signs of syphilis of the central nervous system, while a negative Wassermann reaction was not infrequent in patients with signs and symptoms of activity in the central nervous system.

In patients under therapy for syphilis of the central nervous system the Davies-Hinton reaction often remains positive or doubtful in the spinal fluid after the Wassermann reaction has become negative, and rarely if ever disappears before the Wassermann reaction.

The questions are raised whether the occurrence of a positive or questionable Davies-Hinton reaction in the cerebrospinal fluid of a patient with no signs or symptoms of syphilis of the central nervous system is sufficient for a diagnosis of asymptomatic neurosyphilis, and whether the treatment of patients with syphilis of the central nervous system should be continued until the Davies-Hinton reaction has become negative. It is concluded that neither of these questions can be adequately answered at present, but some evidence is adduced for an affirmative answer to the latter.

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Since the completion of this study we have encountered a case in which the fluid gave a doubtful Wassermann reaction and a negative Hinton reaction. This fluid was from a patient with absent ankle jerks and a history of treatment for positive blood tests ten years previously at another hospital. The only other abnormal finding in the spinal fluid of this patient was the presence of 15 white blood cells per cubic millimeter. The total protein and the colloidal gold reaction were normal.

INADEQUACY OF INJECTION TREATMENT OF HERNIAS*

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THIS paper is concerned with the end results of a four year study of 20 patients who were treated for inguinal hernia by the injection method. Interest in this method was revived in 1930 by Mayer¹ who reported 98 per cent cures in 2100 cases. His results were confirmed by Bratrude² in 1937, but Burdick's³ report in 1937 on 92 patients followed for two years showed failure in all but 3 per cent.

Approximately 50 patients in the clinic began the treatment, but only 20 continued through a full course the others were forced to stop either because of pain following the injections, the annoyance of wearing a truss continuously day and night or occasional untoward reactions. A full course of treatment consisted of some twenty injections, a week or more apart, the number varying from case to case. Adequate treatment was considered to have been achieved when complete fibrosis of the canal was present, the patient could comfortably dispense with the truss and no impulse was detectable. Of the 20 patients, who varied from twenty-eight to seventy five years of age, 10 had direct and 10 indirect hernias. Mayer's solution was used in 11 cases, Sylasol in 5 and Tripoli suspension in 4. All these patients were considered cured at the time of discharge, which occurred at intervals varying from one to two

in these may well occur later. Recurrences, according to some observers are considered to be due to an inadequate number of injections, but in many of our cases the recurrences were so complete and occurred so soon after what appeared to be an adequate degree of fibrosis that a whole new course of treatment would have been required.

Complications were few. Two patients were in shock for several hours after treatment, requiring morphine and emergency ward care. Five had painful cords which persisted for three to five weeks. Nearly every patient had some local pain in 2 cases the patients could not resume work for several days. Two patients had to have emergency treatment for a strangulated hernia, repair of which was more difficult because of the fibrosis and inflammatory reaction.

There are obvious reasons why the injection treatment is likely to fail: the plane of injection is frequently more a matter of conjecture than positive knowledge, so long as the inner lining of the sac is not obliterated the intraperitoneal pressure will sooner or later force the sac through the fibrous tissue, which, like fibrous tissue anywhere, may stretch readily under tension, injection into the sac itself even if possible, is not advisable because of peritoneal reaction and shock.

TABLE 1 End Results

FOLLOW UP PERIOD		HERNIA LAMENT	HERNIA ABSENT
2 yr and 3 mo	0	4	20
2 yr and 6 mo	0	4	16
2 yr and 9 mo	0	6	14
3 yr	0	8	12
3 yr and 3 mo	12	12	8
3 yr and 6 mo	1	1	2
4 yr	18	18	2

years. The follow-up observation period in all of them began two years after the first injection. Table 1 shows the end results after a two-year follow-up period.

The two apparent cures were in one patient with a small indirect hernia and another with a moderate-size direct hernia. Of course, recurrence even

SUMMARY

Twenty patients with hernias were treated by the injection method and carefully followed. At the end of four years 2 patients were cured.

We believe that the injection treatment of hernias is not satisfactory and should be used only when the patient must not be operated on, and then only after the method of treatment and its potentialities for cure have been fully explained to the patient.

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REPORT ON MEDICAL PROGRESS

REGIONAL ANESTHESIA*

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RECENT developments in anesthesia are characterized chiefly by evaluation and selection of methods which the last decade has yielded. One outstanding manifestation of change is the emergence of spinal anesthesia as the most useful type of regional anesthesia, another is the demonstration of its practicability as a substitute for general anesthesia. Methods of regional anesthesia except those of spinal block, have changed but little. There has been a tendency to substitute the newer forms of spinal block for other forms of regional anesthesia, so that consideration of this subject becomes a discussion of the present status of spinal anesthesia.

GENERAL CONSIDERATIONS

No other anesthesia so easily provides widespread muscle relaxation, intestinal quiet and easy recovery as does regional anesthesia. The amount of drug required is extremely small. Preliminary medication is essential to complement the anesthesia by lessening annoyance, inducing psychic calm and dimming memory. This should include a barbiturate to counteract the rare toxic manifestations of the anesthetic. Toxic manifestations, if invoked, occur early and steadily subside. It is not generally believed that there is any advantage in using mixtures of anesthetic drugs.

The usual practice restricts spinal anesthesia to operations below the diaphragm, although it can safely be used by some for intrathoracic surgery. Above the level of the clavicles it produces almost complete paralysis of respiration, and for operations on the neck and head it seems wholly undesirable.

Facilities for providing artificial respiration and supplementary anesthesia must always be available. Spinal anesthesia can prove difficult, even disastrous, for an inept user, and a surgeon cannot safely assume responsibility for both the anesthesia of and the operation on the same patient. The contraindications are really no more than those which apply to all anesthetics, except that children less than seven years old are more manageable under general anesthesia.

The principal disadvantages, in order of their

relative importance, are necessity for observation of the patient throughout operation by a physician thoroughly familiar with the problems of spinal anesthesia, possible occurrence of nausea and vomiting, possible premature termination of anesthesia, possible respiratory paralysis, possible circulatory collapse, possible neurologic sequelae.

PHARMACOLOGICAL CONSIDERATIONS

Investigations^{1, 2} on rabbits have resulted in the following appraisal of the principal drugs:

Concentration in spinal fluid required to effect minimal anesthesia

Pontocaine	0.05 per cent
Nupercaine	0.07 per cent
Tutocain	0.50 per cent
Metycaine	0.86 per cent
Procaine	0.90 per cent

Minimal lethal concentration in spinal fluid

Nupercaine	0.8 per cent
Pontocaine	1.5 per cent
Metycaine	3.5 per cent
Tutocain	6.0 per cent
Procaine	6.0 per cent

Safety ratio (lethal dose to anesthetic dose)

Metycaine	4.1
Procaine	7.1
Nupercaine	11.1
Tutocain	12.1
Pontocaine	30.1

Duration of anesthesia from minimal anesthetic concentrations

Tutocain	11 minutes
Metycaine	13 minutes
Procaine	16 minutes
Pontocaine	25 minutes
Nupercaine	41 minutes

INTRATHECAL DYNAMICS

The specific gravity of normal spinal fluid varies from 1.001 to 1.009. Procaine in spinal fluid forms a solution only slightly heavier than the spinal fluid.³ Its spread in this form depends more on the manner of injection than on gravitational effect.⁴ Because the specific gravity of spinal fluid is not constant, there can be no constant difference between it and the specific gravity of a ready-made solution. If the specific gravity of the anesthetic solution is within the range of that of spinal fluid, the behavior of the former when mixed with the latter cannot be predicted unless actual tests have

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established the nature of the dissimilarity. Such tests have been described^{4, 5} but they seem almost too delicate for routine clinical use. Unless thus tested however, such a solution as 1 per cent Pontocaine (specific gravity 1.007) behaves unpredictably as an anesthetic, since it may be either heavier or lighter than the spinal fluid.

Anesthetic practice indicates increasing preference for solutions with specific gravities quite distinct from that of spinal fluid. Both the light and the heavy solutions can be made to move or remain stationary by appropriate changes in the patient's position.

Of spinal anesthetics, Pontocaine appears to excel in safety and Nupercaine in duration of effect. Measures which provide control of the effects of these drugs have greatly increased the possibilities of spinal anesthesia, and have made it possible to discard other drugs previously used.

ANESTHETIC AGENTS

Procaine

Much of the adverse opinion of spinal anesthesia has arisen from experience with procaine. "Had we been limited to procaine," says Heard,⁶ "we too would have abandoned spinal in large measure, certainly for any procedure over one hour or requiring more than 150 mg."

Nupercaine

Nupercaine is the anesthetic of choice for a lengthy operation. Its effect lasts for two and a half to four hours. Compared with procaine, it produces less circulatory depression and provides prolonged motor anesthesia.^{4, 5}

A light solution of Nupercaine is preferred because of the ease with which it is concentrated at a high level, and the freedom with which the Trendelenburg position can be employed at the onset of the operation. The hypobaric solution is obtained by high dilution (1:1500) of the drug in 0.5 per cent saline solution which gives it a specific gravity of 1.003. It is therefore not invariably lighter than spinal fluid but since 80 per cent of spinal fluids show specific gravities ranging from 1.004 to 1.007, it is usually so. Cases of its proving heavier than spinal fluid have been reported.⁴ In order to avoid this exceptional fault of Nupercaine, it is now being made in a solution with a specific gravity of less than 1.001, and solutions even lighter than water have been devised.

Etherington Wilson⁷ found that in glass tubes simulating spinal canals the rate of ascent of samples of Nupercaine of varying lightness, depends on the angle of inclination, the temperature of the injectum, the speed of injection, the

of the injectum and the difference in the specific gravities of the samples. The vertical position, he found, gives a slower rise than an inclined position near the vertical, and he recommended that the injection be made with the spine perfectly erect, that is, with the patient seated. With the injection made through the third lumbar interspace, his dosage amounts and time intervals are for low anesthesia 10 cc., twenty seconds; for medium anesthesia 12 cc., thirty seconds; for high anesthesia 15 cc., forty seconds.

Ordinary experiences demonstrate that such a solution rises more slowly when the inclination of the spine is less than forty-five degrees from the horizontal than when it is vertical or nearly so. Practitioners in this country prefer a technic which employs this principle and allows more leisurely administration of the anesthetic than does that of Etherington Wilson. Such a technic was proposed by Jones,⁸ and as modified by Woodbridge⁹ provides satisfactory and safe anesthesia. It prescribes a dosage proportional to the patient's height, injection with the patient in a horizontal position, immediate change to the prone position, with the upper chest elevated so that the spine slopes upward from the site of injection to about the fourth thoracic vertebra and downward cephalad from that vertebra. Frequent testing in order to ascertain the progress of the anesthesia, which if slow in developing may be accelerated by increasing the slope and limiting the anesthesia to the desired height by adopting the Trendelenburg position when that height is reached.

The advantages of this technic are these: four to ten minutes, rather than a few seconds, is available for manipulating the anesthetic; the "bubble" behavior of the Nupercaine permits a considerable degree of control; the prone position brings the most intense anesthetic effect to bear on the sensory roots, and one avoids the erect position, which, especially when the patient has been heavily medicated or has deficient powers of circulatory adjustment, is conducive to vascular collapse.

The disadvantages of light Nupercaine are as follows: the large amount of solution (16 to 20 cc.) used and the advisability of having it warm, the relatively slow anesthetizing action, the use of the prone position, which may embarrass respiration or aggravate vascular collapse in obese, arteriosclerotic or debilitated patients (although probably less than does the vertical position), and the occasional case in which the spinal fluid is lighter than the Nupercaine solution.

Such drawbacks keep Nupercaine from being the most serviceable anesthetic for routine use, but when prolonged spinal anesthesia is required it is the drug of choice.

Pontocaine

The development of means of creating a heavy solution of a spinal anesthetic constitutes one of the noteworthy contributions to the progress of spinal anesthesia. Pontocaine solution, made heavy by the addition of 10 per cent dextrose solution, as proposed by Sise,¹⁰ provides unequaled anesthesia for routine use.

Pontocaine, as compared with procaine, is reported as causing less depression of blood pressure,⁶ less nausea and vomiting^{9, 11} and fewer postoperative complications and neurologic sequelae.^{6, 11} Although approximately four times as toxic as procaine, Pontocaine is approximately eighteen times as potent, and therefore gives more intense anesthesia in a dose approximately one tenth that of procaine.

The dosage varies from 8 to 20 mg (0.8 to 2.0 cc of a 1 per cent solution). Abdominal anesthesia in children is obtained with a dose of 1 mg per year of age. The volume of dextrose solution used is always at least equal to the volume of Pontocaine solution, a larger proportion is frequently advisable. Individualization of dosage is possible because the gravity effect persists for several minutes, and varies according to the proportion of dextrose added and the degree and duration of slope adopted. The following cases are illustrative. (1) Sixteen to 20 mg of Pontocaine, plus 3 cc of dextrose solution, injected with the patient in the Trendelenburg position, immediately flows cephalad. By following its progress with testing the anesthesia, and appropriately maneuvering the slant of the table, the Pontocaine is quickly concentrated in the thoracic area and permits upper abdominal surgery for one and a quarter to two hours. (2) Twelve to 20 mg (1.2 to 2.0 cc) of Pontocaine, plus one and a half times as much dextrose solution, injected with the patient level, stagnates around the point of injection and the mixture begins to dissipate. The effect of the Trendelenburg position is then more sluggish, and under it the anesthesia rises slowly and is concentrated in the lower thoracic and lumbar areas, permitting initial abdominal palpation, then lower abdominal and pelvic surgery for one and a half to two and a quarter hours. (3) Eight to 20 mg of Pontocaine, plus 3 cc dextrose solution, injected with the patient in the reverse Trendelenburg position, flows caudad. Maintaining the position concentrates the anesthesia in the lower lumbar and sacral area, and permits operation on the lower urinary tract, external genitalia, perineum and lower extremities for as long as three hours.

The mobility of heavy Pontocaine makes it dangerous unless the cervical spine and head re-

main higher than the level of injection. But this very mobility also makes it the most efficient of spinal anesthetics, capable of ready manipulation during induction and thereafter readily controllable. It enables the anesthetist to vary his methods according to his problems, and makes possible precise placing of anesthesia. The practitioner who always employs the same dose and technic lacks versatility as much as does the surgeon who knows but one method for approaching a surgical problem.

SEQUELAE ATTRIBUTABLE TO SPINAL ANESTHESIA

Untoward effects from spinal anesthesia are becoming less frequent. The principal sequelae now seen, headache, backache and "neuritis," are really those of lumbar puncture. Headache, usually caused by seepage of spinal fluid from the dural wound, is minimized by using a fine needle (24-gauge), making a single puncture and avoiding elevating the head for twenty-four hours. Merely using a fine needle so nearly abolishes headache that patients can comfortably become ambulatory within twenty-four hours.¹² The backaches for which spinal anesthesia can be considered responsible result chiefly from trauma to the periosteum, and may be considerably reduced by careful technic. Backache due to positional strains during operation may develop under any type of anesthesia. "Neuritis" more frequently results from trauma than from drug action. Accurate midline punctures avoid the posterior roots except when, owing to disease or anomaly, there is abnormal fixation of the cauda. Neuritis thus produced by trauma subsides within ten to twenty days unless excessive injury is inflicted.

Complications such as cranial nerve palsies and degenerative cortical lesions have been described.¹³ Schreiber¹⁴ states the modern viewpoint when he ascribes such lesions to cortical anoxia rather than to drug effect, and declares that they are preventable. Similar lesions are seen following nitrous oxide anesthesia with anoxemia.

Peripheral palsies (foot drop and so forth) appear to be most frequent after procaine anesthesia, possibly because highly concentrated solutions of that drug are often used. Lundy et al.¹⁵ showed that concentrations of procaine above 17 per cent are highly destructive to nervous tissues. There appear to be very few, if any, cases of permanent paralysis resulting from the use of Pontocaine or Nupercaine.

Lehman et al.¹⁶ report that patients termed "spinal cases," as compared with "ether cases," convalesce with less nausea, vomiting, distention, headache, backache and general discomfort. Decisive data on pulmonary complications are not available, but

it appears that operations under all anesthetics, including local infiltration,¹⁷ are followed by about the same incidence of pneumonitis and atelectasis. Concurrent or recent infections of the respiratory tract, decreased pulmonary aeration because of pain and clinostatic blood stasis contribute more to their occurrence than does anesthesia.

EFFECTS ON CIRCULATION

In probable order of importance the circulatory mechanisms affected by spinal anesthesia are paralysis of sympathetic vasoconstrictors, loss of massaging action of skeletal muscles, decreased respiratory pumping effect and, under abnormally high anesthesia, respiratory paralysis leading to anoxemia, which unless oxygen is administered leads to respiratory depression and secondary vascular collapse. Seevers and Waters¹⁸ have stated that spinal anesthesia extending up to the midthorax invariably produces enough impairment of respiration to prevent adequate oxygenation of body tissues unless additional oxygen is supplied.

Of these effects, the second and third occur under general anesthesia and are inevitable. The first and fourth, which characterize spinal anesthesia particularly, must be taken into consideration with every administration of a spinal anesthetic.

The hypotension of spinal anesthesia results in large part from extensive vasomotor paralysis, for it does not occur in sympathectomized animals.¹⁹ Its features are quite different from those resulting from shock or hemorrhage. In the case of shock, trauma produces "toxins" or abnormal nerve impulses which cause paralysis and dilatation of the capillaries and venules, an increased endothelial permeability with transudation of plasma, and increased capacity of the vascular system. There follows a generalized compensatory vasoconstriction which is more or less effective in maintaining blood pressure until vasomotor exhaustion occurs. In hemorrhage, there is blood loss, leading to decreased blood volume, passage of tissue fluids into the blood and compensatory vasoconstriction as in shock. Under spinal anesthesia, vasomotor paralysis at the onset leads to increased capacity of the vascular system, and a more or less effective effort of the uninterrupted portion of the vasomotor mechanism to compensate therefor. Hence, spinal hypotension is not analogous to shock, for vasoconstriction is maximal at the onset of shock but minimal, because of paralysis, at the onset of spinal anesthesia. Vasoconstricting drugs are unavailing in shock, but are beneficial in spinal hypotension. CoTui²⁰ found the usual therapy for shock (infusion and transfusion) ineffective in spinal hypotension and vaso-

constrictors the only efficacious remedy. He also found that while in cases of shock the Trendelenburg position relieves the respiratory depression and restores circulation, in spinal hypotension it accomplishes little.

Even gentle manipulation of the abdominal organs almost inevitably stimulates the shock reflex and the patient under spinal anesthesia shows a tendency to develop shock unless specifically protected against it by administration of vasoconstrictor drugs. In adequate doses these wholly abolish spinal hypotension, and when no shocking reflexes are invoked by the operation, normal blood pressure is readily maintained throughout the duration of the anesthesia. If shock develops, vasoconstrictors are needed to enable the paralyzed vasomotor mechanism to exercise its normal protective influence.

If it seems that undue emphasis is being given here to the matter of circulatory changes, the reason is that increasing knowledge of this matter makes possible the extensive application of spinal anesthesia which is here advocated.

Vasoconstrictor drugs

Constant use of ephedrine demonstrates frequent side effects: palpitation, tachycardia, stenocardia, arrhythmia, nausea and retching. Neosynephrin hydrochloride, in a dose of from 1 to 3 mg., is an equally potent pressor substance and appears virtually incapable of upsetting the patient. It typically makes the pulse slower and stronger.

A notion prevails that vasoconstrictors become ineffective after the blood pressure has fallen. Actually, however, because the circulation is inefficient in hypotensive states, the lack of pressor response is chiefly due to delayed passage of the drug from the site of injection into the blood stream. Vigorous massage of the hypodermic deposit almost always promotes a good response, and such massaging should be conducted until evidence of absorption is noted.

Adrenalin is intended by Nature to act in brief emergencies rather than over extended periods, and is a relatively poor vasoconstrictor. It often causes tachycardia especially when the cardioinhibitors have been paralyzed by scopolamine.

Whether the anesthetic itself conditions the vasoconstriction is unknown. The presence of cocaine in a smooth muscle cell is known to augment the adrenalin effect, abolish the ephedrine effect and fail to change the Neosynephrin effect.²¹ If future work shows that our spinal anesthetics resemble cocaine in this respect we may have a more logical basis for selecting vasoconstrictor drugs.

An ephedrine-Pitressin mixture has found some favor. Pitressin, however, is a dangerously potent

coronary constrictor²² Simultaneous administration of ephedrine apparently neutralizes this property,²³ but Pitressin might well be omitted, lest the unwary, ascribing to it some particular virtue, err in using it without the ephedrine

CONTRAINDICATIONS

The contraindications of spinal anesthesia have so decreased that now, if it be appropriate for use during the proposed operation, some surgeons and anesthesiologists with large experience believe that is the method of choice regardless of the condition of the patient^{24 25}

The traditional infiltration anesthesia for poor-risk patients compares unfavorably with spinal anesthesia for these reasons: the longer time needed for induction, the larger amount of drug injected, the inconvenience and danger of multiple injections, the possibility of intravenous injection, the difficulty in obtaining complete anesthesia, the brief duration of anesthesia, the fact that shock reflexes are still provoked by pain and manipulation of viscera, the failure to reduce intestinal distention, the possibility of evisceration during retching or vomiting, and the difficulty of placating the patient made uncontrollable by operative distress

The patient in shock is a poor-risk patient, but if his blood pressure is still adequate, vasoconstrictors will maintain it under spinal anesthesia. If on the other hand vasomotor collapse has already occurred, spinal anesthesia can hardly make the situation worse. It is known that strong pain stimuli are a factor in causing shock, and O'Shaughnessy and Slome²⁶ found spinal anesthesia the only measure capable of raising blood pressure in animals in shock from severe trauma to the lower extremities

Under inhalation anesthetics, internal respiration is impaired to whatever extent the blood is compelled to transport anesthetic rather than oxygen and carbon dioxide. When tissue vitality is low, as in shock, the entire oxygen-carrying capacity of the blood might better be kept available for oxygen-carrying

For an operation on the poor-risk patient, infusions and transfusions are employed, a vasoconstrictor is administered, then spinal anesthesia, and an oxygen atmosphere is provided to prevent or combat the anoxia of toxemia and vascular collapse. This regime often improves the patient's condition even while the operation is in progress, and seems so rational and advantageous that one regrets that it is not applicable to every situation

No doubt the most peculiarly unsuitable subject for spinal anesthesia is the patient with severe combined atherosclerosis and arteriolar sclerosis. This

disease makes circulatory adjustments inefficient: the arterioles cannot change much in caliber, the aorta cannot initiate normal pressor reflexes, and vasomotor stimulation is relatively impotent. Such persons experience cerebral anoxia (vertigo) even when they rise quickly. They develop shock from minor trauma, for they have no effective vasomotor mechanism to compensate for capillary dilatation and stagnation. Time spent in administering stimulants to such patients when circulatory collapse occurs would be spent much more profitably in administering oxygen and lowering the head

Faith in various analeptics as panaceas for anesthetic crises is often unfortunate. Stimulants or the time spent in administering them may distract an anesthetist long enough to give the patient time to die, and in a crisis a patient may die with stimulants more quickly than without them, if oxygen alone is administered. Picrotoxin, Metrazol and Coramine are worthless for treating the circulatory or respiratory depression resulting from spinal anesthesia per se²⁷; adrenalin may cause death, especially when given in the heroic dose which an emergency easily inspires, Pitressin alone is wholly bad

* * *

In all operations for which the use of subarachnoid block is appropriate, it has been found to be a suitable form of anesthesia. Its proper conduct requires an anesthetic solution which can be controlled within the spinal canal, and a thorough knowledge of the circulatory-respiratory phenomena which occur under spinal anesthesia, together with facility in handling them intelligently

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 25491

PRESENTATION OF CASE

A forty-year-old garage owner was admitted to the hospital complaining of recurrent episodes of painless jaundice

Four years before entry the patient's wife first noticed the appearance of jaundice, which gradually deepened and was associated with foul, clay-colored stools, amber-colored urine, generalized pruritus and frequent nosebleeds lasting ten to fifteen minutes each. He also became nervous, irritable and tired and had low abdominal pain following the ingestion of fried foods, cream and ice cream sodas. His appetite, however, remained excellent. There was no right upper-quadrant pain, nausea or vomiting. This apparently passed after a few months, and he was seemingly well until about two and a half years before entry when he was treated by a physician for left otitis media following an upper respiratory infection. At this time it was also noticed that he had marked jaundice, that the liver was enlarged, but not tender and that there was a return of the symptoms which had accompanied his previous attack of jaundice. He was put to bed for six weeks and placed on a fat-free diet with bile tablets. On this regimen, the jaundice, pruritus, nervousness and irritability temporarily lessened, and the liver receded. After returning to work he noted an extraordinary susceptibility to cold, although he denied having chills. Eleven months before admission he noticed, for the first time, a swelling of the left ankle. Six months before entry he could not button his vest over his upper abdomen, his jaundice increased markedly, and he became drowsy much of the time. His ankles and legs became swollen but were normal when recumbent. Clay-colored stools, which waxed and waned in intensity (at times the stools were of normal color), and frequent nosebleeds reappeared and he bruised easily. These symptoms increased gradually so that he had difficulty in pulling his trousers over his legs. He became dyspneic on exertion and was deeply jaundiced, so much so, that on entering an outside hospital for treatment one week later he was given Chinese rice for his first meal by the hospital attendants. At this time he was often awakened at night gasping for breath, with a feel-

ing of tightness and oppression in his chest and of a "filled-up" abdomen. He remained in the hospital for two weeks where he was given digitals and diuretics, with the result that the peripheral edema markedly decreased and the jaundice lightened. These symptoms recurred on discharge, however, so a few days later he was admitted to this hospital for further study.

The patient had worked in the garage business for fifteen years. Only recently had he used a gasoline which was said to contain 15 per cent benzol. The family and marital histories and the remainder of the past history were non-contributory.

Physical examination revealed a well-developed and nourished, moderately jaundiced man who was in no acute distress. There were a few scratch marks and small ecchymotic areas scattered over the yellow skin. There was a blood crust over a recent bleeding point in one nostril. The neck veins were not distended, and he could lie almost flat without discomfort. The chest was normal, but the diaphragms were high. The heart was percussed 1 to 2 cm. beyond the midclavicular line in the fifth interspace. The sounds were of fair quality, the rhythm regular, and the rate 88. A blowing systolic murmur was heard over the apex and pulmonic area. The blood pressure was 140 systolic, 70 diastolic. The abdomen was bulbous, with "moderate ascites." The liver edge was palpated 6 cm. below the costal margin, but the spleen was not felt. The lower legs and feet were moderately edematous.

The temperature was 99°F, the pulse 88, and the respirations 20.

Examination of the dark amber-colored urine revealed a specific gravity of 1.018, with + albumin and a ++++ bile test; there were rare granular casts, rare red cells and occasional white blood cells in the sediment. One stool was brown and soft-formed, another, gray. The blood showed a red-cell count of 2,920,000 with 86 gm. hemoglobin (photoelectric-cell technic), and a white cell count of 13,900 with 84 per cent polymorphonuclears. The serum bilirubin by the van den Bergh test was 14.4 mg. per 100 cc., biphasic, and the icteric index approximately 90. The serum nonprotein nitrogen was 18 mg. per 100 cc., the serum protein 6.8 gm. The serum chlorides were equivalent to 90.6 cc. of N/10 sodium chloride per 100 cc., and the carbon-dioxide combining power 23.3 cc. of N/10 carbonic acid, both on the thirteenth hospital day. A phenolsulfonephthalein test showed 50 per cent excretion, 30 per cent in the first thirty minutes. An electrocardiogram showed a ventricular rate of 85, with normal rhythm, a low, slightly diphasic T₁, a sagging ST-

an inverted T_2 and a low diphasic T_4 , R_4 was upright. Roentgenograms of the chest showed high diaphragms and hazy linear densities at both bases. Both costophrenic angles were obliterated by small amounts of fluid. The heart shadow was considerably increased in size, the enlargement being almost entirely in the region of the left ventricle. The aorta was tortuous but showed no evidence of dilatation. The esophagus showed no evidence of varices. The blood Hinton test was negative.

The patient ran an uneventful course, with normal temperature, pulse and respirations, for the first eight days in the hospital, except for pain on defecation and the passage of a few ounces of bright-red blood which apparently came from slightly enlarged internal and moderately enlarged external hemorrhoidal veins and from two or three small external fissures. The rectum was treated with lubricants and 2 per cent tannic acid compresses, with relief. A bleeding point in the nose had to be cauterized. He was placed on a high-carbohydrate, high vitamin high-caloric diet with bile salts and parenteral administrations of glucose. He was given chloral hydrate, digitalis ($1\frac{1}{2}$ gr twice a day), liver extract (intramuscularly) and thiamin chloride and was transfused.

Attempts to reduce the edema and ascites with Salyrgan were of little success. On the tenth hospital day the temperature, pulse and respirations rose to 100.5°F ., 120 and 30, respectively. He became somnolent, very weak and dyspneic. A few rales appeared at both bases. Both spider angiomas and a mousy breath were noticed. He gradually failed and died on the sixteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD J. CLARK I should like to ask if the tortuosity of the aorta and apparent cardiac enlargement may not have been due to high diaphragms.

DR. OTTO SAHLER Yes, the belief was that the heart was not much increased in size. The most important thing from your point of view is that there was no definite evidence of varices in the esophagus.

DR. CLARK I take it there were no films of the gall bladder region.

DR. SAHLER No.

DR. CLARK Apparently this patient was very sick and not put through a very extensive course of study. I think we may start with the assumption that he had some type of fairly severe liver disease, which eventually proved fatal. One question which arises is the relative importance of the cardiorespiratory symptoms. Did the heart have anything to do with his condition? It probably did not. I think the cardiac enlargement which

the patient showed was in considerable part due to the high diaphragms. He may well have had some dilatation and some myocardial weakness as the result of secondary anemia. The electrocardiogram did show some T wave changes, but these can well be accounted for on the basis of anemia or the digitalis which he had received. I do not believe he had serious coronary heart disease. His blood pressure at the time of entry was quite normal, perhaps it was a little higher than one would expect in a man in a debilitated state, and this makes you wonder if in the past he had had a somewhat elevated blood pressure which may have produced left ventricular hypertrophy of the hypertensive type. We do notice that he was able to lie flat in bed and had no distention of the neck veins, and that is of considerable significance. Whatever he may have had in the heart in this connection is a side issue and had nothing to do with the primary situation.

Let us come back to four years before entry, at the beginning of this history, when we find a man with painless jaundice of the obstructive type, which came on apparently rather gradually, we have no definite clue as to what this was. We might first think of catarrhal jaundice, but it is surprising that he had a good appetite all the way through. We wonder about the possibility of a silent gallstone. I see no reason why this might not explain the primary picture. He might have slipped the stone back into the gall bladder in the course of time or passed it out. On the other hand, the foul clay-colored stools are significant and make me wonder about the pancreas. Were these "pancreatic stools," and did he have some degree of pancreatitis at that time? He did not have much pain, but in a very low-grade pancreatitis there might be little more than the lower abdominal pain described. The fact that the jaundice continued for several months—we do not know just how long—is more in keeping with a diagnosis of pancreatitis than with that of a stone which had passed.

He then got along fairly well. We are not told whether the jaundice completely disappeared. My guess would be that it subsided largely but that he had some trace left. Two and a half years before entry he developed an acute respiratory infection and at that time was found by a physician to be markedly jaundiced and to have some enlargement of the liver. As the disease progressed we find about eleven months before entry evidence of circulatory obstruction—first a swelling of the legs, and later, ascites. The fact that his vest would not button over the upper abdomen makes me wonder whether it was because of an extremely large liver or ascites. It might

have been either, but I presume it was an indication of developing ascites. From this time on the jaundice remained quite intense, but there was evidence of only intermittent complete biliary obstruction. After he entered the hospital his stools were at times dark and again clay colored, this is a fairly significant fact. In spite of vigorous treatment of the cardiovascular symptoms and the liver disease, he ran a progressively downhill course and died with what apparently was complete liver failure and possibly a terminal pneumonia.

How can we fit this picture together? The first thing we think of is ordinary portal cirrhosis of the Laennec type. Many things make this improbable. He started with jaundice early in the course of the disease and showed marked jaundice before he had ascites, facts which are out of keeping with such a diagnosis. He had no evidence of esophageal varices, no story of dilated veins in the abdomen, no history of alcoholism and no splenic enlargement. In view of these facts I shall rule out ordinary portal cirrhosis.

The next consideration would be Hanot's hypertrophic cirrhosis. This is rather a rare condition and occurs primarily in young people. Statistically he is just under the age limit for this. It is more apt to occur at thirty or under. Hanot's cirrhosis would explain the early deep jaundice which later went on to evidence of portal obstruction. However, in Hanot's cirrhosis I think one is rather more apt to get a progressive, continuous jaundice than an intermittent jaundice. Furthermore, in Hanot's cirrhosis one is apt to get bouts of fever, of which there is no evidence here, and splenic enlargement is almost universal. If we are to believe the physical examination he had no enlarged spleen. It is possible with the ascites that the spleen might have been missed.

Syphilis could produce a picture similar to this, but on the basis of the negative serological test we have to rule this out. Familial jaundice might be considered. It is not infrequently associated with gallstones. Against this is the lack of a family history, the relatively mild anemia and the absence of splenomegaly.

We are told about his occupation, and that he was exposed to benzol but only for a short time. It does not say how long. Certainly the benzol could not have had anything to do with the picture in the beginning. He was a garage man and he might have come in contact with lead. So far as I know lead could not produce this picture. I do not believe garage men are in contact with phosphorus. I am going to dismiss any occupational cause for his disease.

Then one comes down to the conditions which

can produce ascites and jaundice without splenic enlargement, and perhaps the most common of these is metastatic cancer of the liver, which is not infrequently from a focus undetermined *ante mortem*. One might also consider a primary cancer, either in the bile ducts, liver or pancreas, or any one of the lymphomas giving obstruction in the portal area. I shall rule all these things out for the simple reason that the jaundice was intermittent. If he had had any type of tumor which pressed on the bile ducts and caused jaundice, it would be most unlikely for the bile ducts to open up and pass bile on one day and shut down and fail to pass bile on another.

The one condition that I can think of which might produce this picture is the so-called "obstructive type" of biliary cirrhosis, and I believe that is what this man had. I think it may well have been based on a chronic, low-grade pancreatitis and infection in the bile ducts, which had been continuing off and on ever since the first bout four years previously. We might fairly consider whether he had gallstones as well, it would not be at all surprising if this were the case, but we have no positive evidence for them.

In addition to the obstructive biliary cirrhosis, there must have been a secondary generalized fibrosis of the liver giving rise to portal obstruction.

DR TRACY B. MALLORY: Are there any other suggestions? Dr. Bishop, you saw this patient in life. Have you any comment?

DR WILLIAM A. BISHOP: I know more of his history than the record states. He said that his lower abdominal pain always accompanied protrusion of a small hernia in the left inguinal region, this was indirect in type. He was convinced that that was the source of his trouble, but I never believed it could possibly have any bearing on his troubles because he had pain when lying down with the hernia in. He said if he got up in the morning with it out and went to work he was sure to have abdominal pain.

When I first saw him he had a clinically enlarged heart and murmurs, and I wondered if we were dealing with chronic passive congestion. I gave up that idea when we got x-ray films that did not show right-sided cardiac insufficiency. Yet I clung to that explanation for a long time. I thought of cirrhosis of the liver as a possibility. I agree with the speaker on the question of benzol. His only exposure was to a benzol type of gasoline that he was delivering to cars. It is my opinion that garage men—and statistically it has been shown—are not troubled with benzol or lead poisoning from the delivery of benzol or tetra lead gasoline, so we ruled out occupation as a cause of his illness.

One or two other things were interesting. When I first saw him in the Concord Hospital he showed edema of the feet and legs and there seemed also to be some fluid in the abdomen but no definite ascites. This disappeared with rest and digitalis, and that lent a little more color to my first impression of cardiac insufficiency. He complained of night blindness and was successfully treated with large amounts of vitamins. He stated that he could stare at a glaring headlight without the dazzling effects that most of us experience. Amblyopia was another interesting complaint, which was, of course, connected with his jaundice, that too disappeared while in the Concord Hospital.

Dr. MALLORY Dr. Bishop, will you continue and tell about the peritoneoscopy.

Dr. BISHOP That showed a definite hobnail liver, which seemed to be an adequate explanation for both the portal and biliary obstruction. We still had no clue as to why he had this condition. He was not an alcoholic. In fact he said that the amount of alcohol he had drunk in his life "you could put in your eye."

CLINICAL DIAGNOSES

Cirrhosis of liver, with superimposed acute hepatic failure

Dr. CLARK'S DIAGNOSES

Obstructive biliary cirrhosis.
Secondary portal fibrosis, with ascites
Hepatic failure.
Chronic pancreatitis
Cholelithiasis and cholecystitis?
Terminal pneumonia?
Left ventricular hypertrophy?

ANATOMICAL DIAGNOSES

Cirrhosis of the liver, toxic type, with acute hepatitis
Hypertrophy of the heart, slight
Splenomegaly
Bile nephrosis
Arteriosclerosis, slight aortic and coronary
Icterus
Ascites

PATHOLOGICAL DISCUSSION

Dr. MALLORY This is the type of case in which peritoneoscopy can be very useful. The problem here was whether the disease was purely intrahepatic or whether there was also an extrahepatic element for which surgery might possibly have offered something. The demonstration of a really nodular liver by peritoneoscopy settled the point and obviated any necessity of an exploratory laparotomy.

I personally disagree with the description that it was a hobnail liver. This matter came up a few weeks ago and the question was raised, What is the size of a hobnail? I have never seen hobnails that were more than 4 mm across. The lumps of nodules on the surface of this liver were much bigger—10 to 15 cm in diameter. Therefore I should rather call it a nodular liver than a hobnail liver. A hobnail liver is very characteristic of alcoholic cirrhosis and is not commonly seen in other types of portal cirrhosis, one of which I think we have to say this man had. His liver was still big at the time of autopsy, weighing about 2000 gm. It was very grossly nodular, and extremely tough and fibrous. On microscopic examination there was extensive cirrhosis with large bands of fibrous tissue containing innumerable bile ducts, the type of picture we frequently see in subacute and acute atrophy. There were foci of progressive acute necrosis in the liver even at the time of death.

There are many things about the case that I do not know how to answer. Whether this had been a steadily progressive process for all four years or whether it occurred in two or more separate and definite episodes, I do not know, though my temptation is to think that it was probably a slowly progressive affair. As to the etiology we have absolutely no lead. Pictures rather like this have been seen in cases of catarrhal jaundice that have been traced through from the acute stage to the final development of severe cirrhosis. Such a course of events is certainly unusual but there is no question it can happen.

Dr. Clark based part of his argument on the fact that the spleen was not enlarged and there he was misled because the spleen was quite big but had not been felt. It weighed 550 gm and should have been felt without difficulty. There was only slight hypertrophy of the heart, it weighed 400 gm. The coronary arteries showed a little sclerosis with no significant narrowing. The kidneys, as is customary in jaundiced cases, were considerably enlarged and showed what could be described as bile nephrosis. The lungs showed terminal edema but no significant amount of pneumonia.

Dr. RICHARD SWEET I should like to have you comment a bit on chronic pancreatitis. I have been impressed by the fact that it now enters much less into the differential diagnosis of obstruction of the common duct than it formerly did. Dr. Daniel F. Jones frequently performed biopsies of the pancreas when he thought there was a chronic pancreatitis. Nowadays you hear very little about it.

Dr. MALLORY For some fourteen years we

have been putting through routine sections of pancreas on nearly every autopsy, and we find a chronic pancreatitis in less than 1 per cent of the cases. Of all the various organs of which we make microscopic sections, the pancreas is the least apt to show anything of interest. I personally believe that chronic pancreatitis is an extremely rare condition. It used to be considered relatively common, and I think the probable explanation was that the surgeon, feeling of the pancreas, felt something very hard. He only felt the pancreas on occasions when he was suspicious of it, and the pancreas is much harder than any other organ in the body. The normal pancreas feels as hard as inflamed or almost as hard as neoplastic tissue in any other organ so that it is almost impossible, I think, to make a diagnosis of chronic pancreatitis by palpation.

DR SWEET: I think that is quite true and hoped you would bring it out. The other point is, Does it cause long-standing common-bile-duct obstruction? I doubt it.

DR MALLORY: I am sure it very rarely does. I can conceive of its doing so, however. The relation of the common duct to the head of the pancreas is quite variable. Sometimes the common bile duct is actually buried in the head of the pancreas for a short distance and theoretically could be obstructed.

DR CLARK: Was there any evidence of inflammation in the lower bile ducts?

DR MALLORY: No, nothing to suggest it. The gall bladder was negative.

DR EDWARD A. GALL: Do you believe the anemia was the result of liver disease?

DR MALLORY: I should think so. I do not believe we have to assume any benzol poisoning.

CASE 25492

PRESENTATION OF CASE

A twenty-four-year-old housewife was admitted to the emergency ward complaining of a severe throbbing headache of three hours' duration.

The patient had been apparently well until nine days before admission when she noted the onset of sore throat and an accompanying severe toothache in the region of the right lower jaw. She consulted a dentist who performed an extraction seven days before entry. There was subjective relief of pain, but until admission the tooth socket continued to ooze blood, in spite of frequent wound packings by the dentist, and the use of a liquid medicine which he had prescribed. Five days before entry the sore throat became more severe, and likewise continued until admission. She was seen by a physician three days be-

fore entry who, it was alleged, gave her a small pill every hour "to prevent blood poisoning." Three hours before admission the patient developed a severe headache, associated with a steady decrease in vision.

The patient had been in good health until the present illness. She had two normal children three and four years of age. An appendectomy was done in an outside hospital one year before entry, without undue bleeding. The patient denied the use of drugs of any sort.

Physical examination revealed a sallow, moaning woman who lay restlessly in bed. There were numerous ecchymoses scattered over the body, the largest measured 5 by 5 cm and was located over the right anterior superior iliac spine. The lips were partially everted, dry and covered with exudate. The gums were swollen and purple, and oozed red blood. The tongue was coated, and the tonsils were huge. There were a few tender shotty cervical lymph nodes. The neck was stiff, but the Kernig sign was negative. There was 1 diopter of papilledema of the left eye, and an absent physiological cup on the right. Examination of the heart, lungs, abdomen and extremities was not remarkable.

The urine was grossly bloody. The blood showed a red-cell count of 2,200,000 with 45 per cent hemoglobin, and a white-cell count of 320,000. The stained smear contained many lymphoblasts, no polymorphonuclear cells were seen.

The patient quickly failed, went into coma and died two hours after admission.

DIFFERENTIAL DIAGNOSIS

DR JOHN R. GRAHAM: The diagnosis of the fundamental disorder in this case is presented to us in the next to the last paragraph of the history. Here it is stated that the white-cell count was 320,000 and that the stained smear contained many lymphoblasts. This statement combined with the history of generalized purpura, spongy bleeding gums, sore throat, huge tonsils and a rapidly developing, fatal illness in a woman of twenty-four, makes the diagnosis of acute lymphatic leukemia practically certain.

The manner in which death occurred and its cause leaves room, however, for speculation. It is obvious from the severity of the headache, the failing vision and increasing coma and the early choking of the optic disks that the terminal lesion was within the cranium. The extreme suddenness of the onset of headache, the rapidity with which neurologic symptoms and signs developed and the stiff neck are all typical accompaniments of subarachnoid hemorrhage. Such a hemorrhage would fit in well with the severe bleeding

tendency which had already produced generalized purpura and bloody urine. The question arises as to whether the seat of the hemorrhage lay in a leukemic lesion in the brain or whether it occurred in normal brain tissue as a result of the generalized bleeding tendency. Another remote possibility is that she bled from a congenital aneurysm of one of the intracranial vessels. It is impossible to state just which of these mechanisms was responsible for the hemorrhage, but we can be reasonably certain that it was hemorrhage that dealt the terminal blow. Since the hemorrhage was obviously fairly brisk, one is led to think that it probably came from a vessel of fair caliber. If such was the case the walls of the vessel very likely will show leukemic infiltrations. In any event one is fairly safe in predicting leukemic infiltration along intracranial nerve sheaths or vessels in cases of this kind, since it occurs in a very high percentage of them.

CLINICAL DIAGNOSIS

Lymphatic leukemia.

DR. GRAHAM'S DIAGNOSES

Acute lymphatic leukemia

Subarachnoid hemorrhage.

Leukemic infiltration of intracranial nerve sheaths or vessels

ANATOMICAL DIAGNOSES

Leukemia, acute lymphatic.

Leukemic infiltration of the meninges.

Normal pregnancy

Hepatomegaly

Splenomegaly, slight

Pharyngitis.

PATHOLOGICAL DISCUSSION

Dr. TRACY B. MALLORY. This patient entered the hospital in extremis and died within two hours

of entry. It was therefore impossible to work her up very thoroughly, but as Dr. Graham has pointed out, the white count alone was adequate to establish the diagnosis and the only problem was as to the mechanism of death and the distribution of the lesions. One anatomical finding which would unquestionably have been determined clinically by a more complete and leisurely physical examination was that she was between three and four months pregnant. This may or may not have had a bearing on the course or outcome of the disease. The other obvious features of the gross findings were marked enlargement of the liver, moderate enlargement of the spleen and a general lymphadenopathy. Scattered petechial hemorrhages and ecchymoses were present in the internal organs as well as in the skin. On examination of the brain an intracerebellar hemorrhage in the left cerebellar hemisphere was found, with diffuse hemorrhagic infiltrations of the arachnoid over the entire cerebellum. It was not possible in gross to decide whether this was merely a hemorrhage due to the generalized purpuric state or was secondary to a leukemic infiltration of the meninges. Microscopic examination proved the latter to be the case and substantiated Dr. Graham's suspicion of intracranial extension of the leukemic process.

The frequency of central nervous-system involvement in lymphoma as in leukemia has not been generally recognized. Viets and Hunter¹ reported several cases from this hospital a few years ago in which the lesions were verified at postmortem examination. Somewhat more recently Schwab and Weiss² analyzed the clinical records of 334 cases of leukemia and found neurologic signs indicating central nervous-system involvement in 20.5 per cent.

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The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

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SUBSCRIPTION TERMS \$6.00 per year in advance postage paid for the
United States, Canada \$7.04 per year \$8.52 per year for all foreign coun-
tries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon
on Saturday

THE JOURNAL does not hold itself responsible for statements made by any
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COMMUNICATIONS should be addressed to the *New England Journal of
Medicine* 8 Fenway Boston Massachusetts

PAYMENT FOR MEDICAL SERVICES

THE multiplicity of plans to enable those with low or moderate means to meet the costs of medical care is indicative of the urgency of this problem. Schemes have been devised by insurance companies, consumer groups, physicians and county and state medical societies, particularly within the past few years when economic depression has accentuated so-called "medical indigency" and the financial burden of unpredictable illness and when agencies outside the medical profession have demanded that the problem be recognized and met.

The need for such a provision has been acknowledged by the House of Delegates of the American Medical Association, but nothing official has been said as to the best way of accomplishment, other than the recommendation that any plan should be on a voluntary and cash-indemnity basis. As a matter of fact, it is unreasonable to expect that

a single scheme would be suitable for all states, and it seems not unlikely that in the same state a plan devised for an urban population would not be ideally applicable to those residing in a rural community. However, county and state medical societies in numerous states have promulgated medical-service plans, and some are even in operation. One state-wide scheme—that sponsored by the California Medical Association—has not as yet been enthusiastically received by the public. Another—that of the Michigan State Medical Society—is about to be put into operation.

At a special meeting of the Council of the Massachusetts Medical Society, held last spring, action was taken on the recommendations of the Subcommittee on Social Legislation and Insurance relative to plans which had been submitted for consideration to the Committee on Public Relations. By far the majority of the time was taken up with the discussion, and eventual approval, of a plan whereby the Society was to take the initiative in the formation of a corporation, non-profit in character, which would pay the costs of medical care of patients, and the Committee on State and National Legislation and the Committee on Public Relations were authorized to seek legislation providing for a system of medical-cost insurance. The latter step was taken, but the proposed bill was submitted, of necessity, so late in the legislative session that it was refused admission by the Committee on Rules of the Legislature.

Among other things considered at this meeting was the recommendation by the subcommittee that a plan submitted by Health Service, Incorporated, to supply medical care to people whose maximum incomes were not over \$3000 a year be disproved. The suggested action was based on three objections: interference with the free choice of physicians, the implication that such medical service would emanate from a certain Boston institution, and the failure of the representatives of the proposed corporation to admit that a fee schedule should be arrived at only after consultation with the local medical societies. The recommendation of the subcommittee was accepted by the Council.

In this issue of the *Journal* appears a state

nent by five members of the Massachusetts Medical Society relative to the furnishing of medical care to those who subscribe to a prepayment medical-service plan of a charitable corporation—Health Service, Incorporated. If this corporation is identical with the one whose plan was disapproved by the Council,—and no statement is made to the contrary,—one may reasonably ask, what steps have been taken to meet the previous objections and why was the presumably revised plan not submitted to the Society for approval?

Be that as it may, the need for some method for the family of low or moderate means to budget for the costs of medical care is paramount, and any plan for filling this need should be welcomed by the members of the medical profession provided it is legal and ethical. It remains to be seen whether, according to properly qualified authorities, the medical service offered by Health Service, Incorporated, fulfills these conditions. If so its plan and those of similarly incorporated groups, as possible means of solving one of the most urgent problems with which the medical profession is confronted, should receive the sympathetic interest and the co-operation of physicians.

DEALING IN FUTURES

THE world of tomorrow is something which catches the imagination of all of us at some particular time. We like to envisage its planes and its contours, the achievements of science, and the perfections of man which will fashion the terrestrial realm nearer to our idea of Utopia. We hope that the world of tomorrow will be a better place to live in than the world of today—that our experience and that of those who have gone before us will have smoothed out the rough places for our children and for our children's children.

From out of the box of Pandora, disease came to blight the hopes and happiness of mankind. In our world of tomorrow each one of us would want to reduce suffering and illness to the least possible minimum. At this time of year we have an opportunity to be practical about that desire.

It is one thing to wish and another to do. Christmas Seals are now on sale, Christmas Seals which have sponsored a movement for many years to bring about a worthy goal—the gradual eradication of tuberculosis. The world of today is still struggling against a powerful enemy in this dread disease; the world of tomorrow need have none of it, if we have a real desire to conquer tuberculosis. Buy Christmas Seals!

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

FATAL PUERPERAL INFECTION FOLLOWING NORMAL DELIVERY

Mrs. M. D., a twenty-five year-old para I at term, was admitted to the hospital shortly before midnight on November 28, 1938, in active labor.

The family history was not obtained. The patient's past history was uneventful. Catamenia had begun at twelve and were regular, with a twenty-eight day cycle. Her last period began on February 15, making November 22 the expected date of confinement. Her pregnancy had been supervised in the prenatal clinic and had been entirely normal.

On admission a hasty physical examination showed a well-developed and nourished woman apparently in good health, although her temperature was 100°F. The pulse was of good volume and tension, with a rate of 80. The blood pressure was 120 systolic, 60 diastolic. The throat was normal. The heart was normal, there were no murmurs. The lungs were clear. Abdominal palpation showed a vertex presentation in an LOA position. The fetal heart was heard in the left lower quadrant; the rate was 130. Rectal examination showed the os to be fully dilated and the head at the outlet.

The patient delivered herself normally of a 6 pound 12 ounce, living female child at 12:15 a.m., November 29. The placenta followed ten minutes later and appeared to be intact. A second

* A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

degree laceration was repaired with No 2 chromic catgut. The patient was put to bed in good condition, with the temperature still 100°F.

The temperature had dropped to 99°F the following morning, but rose again to 100 that evening, with a pulse rate of 112. On the second and third days the temperature and pulse were normal, and the patient appeared to be in a satisfactory condition. On the evening of the fourth day the temperature rose to 100.2°F, and on the sixth day to 103, the pulse rate going up to 120. Examination at this time showed a tender fundus and slightly foul pads. A blood culture was negative. The white-blood-cell count was 18,000 and the red-cell count 3,200,000.

Treatment with sulfanilamide was started with the rise of temperature on the fourth postpartum day, and 90 to 120 gr were given daily through the seventeenth day. It cannot be said that the sulfanilamide had great effect on the course of the infection. Determinations of the concentration of the sulfanilamide in the blood were made at intervals of a few days. Beginning at 9.8 mg per 100 cc it ran up to 18.3 mg on the seventeenth day. At that point the administration of sulfanilamide was stopped temporarily.

On the eleventh postpartum day, the red count having fallen to 2,250,000 and the pulse and temperature remaining elevated in spite of the continuous administration of sulfanilamide, the first of a series of small transfusions was given. This was followed by a marked improvement in the patient's general condition and a definite drop in the temperature and pulse rate. This improvement was only temporary, however, and repeated transfusions were given after intervals of two days.

On the eighteenth day the temperature rose to 104.6°F, and the pulse rate to 140. Another blood culture showed no growth. The white-cell count was 17,100, and the red-cell count 2,200,000. Vaginal examination showed a uterus that was fairly well involuted, slightly tender vaults but no masses. The urine showed a large trace of albumin. The sediment contained 3 to 4 white blood corpuscles per high-power field. A consultation was held with an internist who found nothing abnormal in the chest.

After the fourth transfusion on the nineteenth day, there was a considerable improvement in her general condition. The temperature and pulse were lower for several days, and the red-cell count rose to 3,000,000. This improvement lasted nearly a week. On the twenty-sixth day, after the temperature had been normal for twelve hours, the patient had a severe chill. The temperature

rose to 102°F, and the pulse rate to 90. The white-cell count fell off to 7,200, and the red-cell count to 2,600,000. Another blood culture was taken, which showed no growth. Vaginal examination showed a purulent vaginal discharge and some induration in both broad ligaments. The uterus was well involuted. The urine contained a trace of albumin. The sediment showed 20 to 30 white blood corpuscles per high-power field. A second consultation was held with an internist. This observer found that a loud systolic murmur had developed over the precordia, transmitted to the axilla. Many rales were heard over the bases of both lungs.

Sulfanilamide was started again, 90 to 120 gr being given during the next three days. Four more transfusions, varying from 240 to 450 cc, were given during the next ten days. From this time on, however, the patient became steadily worse.

A cystoscopy and pyelography were done on the thirty-fifth day because of some urinary symptoms and persistent pyuria. The left ureter was found to be anomalous, with a non-obstructing constriction at the brim of the pelvis. The right ureter was slightly dilated. An x-ray film showed considerable enlargement of the liver.

After each of the transfusions there appeared to be a slight but transient improvement, but the infection continued. During the last forty-eight hours of life, chills recurred with great frequency. The chest showed many rales, breathing became quite rapid, the pulse steadily grew more rapid and weaker, and the temperature rose to 104°F. Death occurred on January 6, thirty-eight days post partum. An autopsy was refused.

Comment. A patient who enters the hospital with a temperature of 100°F, who delivers herself normally with no instrumentation, who has no postpartum hemorrhage and in whom a fatal puerperal infection develops is proof that such infection is not always caused by "introduction of an organism from without." Since no uterine culture was taken and since the blood cultures were negative, sulfanilamide was used empirically rather than intelligently, this, in a way, is unfortunate for it is well known that the drug has no value except in those infections which are caused by hemolytic streptococci.

This case was treated intelligently from the standpoint of conservatism. The uterus was left entirely alone. In spite of all supportive measures, the infection went on to a fatal termination. If permission for an autopsy had been given, valuable information might have been obtained.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning December 11

MAINTABLE

Sunday December 17 at 4:00 p.m., at the Cape Cod Hospital Hyannis. Pneumonia. Instructor Earle M. Chapman. Donald E. Higgins, *Chairman*

BRISTOL NORTH

Thursday December 14 at 4:00 p.m., at the Morton Hospital Taunton. Head and Spine Injuries. Instructor Walter R. Wegner. Lester E. Butler, *Chairman*

BRISTOL SOUTH (New Bedford Section)

Friday December 15 at 4:00 p.m. at St. Luke's Hospital New Bedford. Indications for Cesarean Section. Instructor Raymond S. Titus. Robert H. Goodwin, *Chairman*

BRISTOL NORTH

Friday December 15 at 4:30 p.m., at the Lawrence General Hospital Lawrence. Pneumonia. Instructor Chester S. Keefer. John Parr, *Chairman*

BRISTOL SOUTH

Tuesday December 12, at 4:00 p.m., in the Conference Room of the Salem Hospital Salem. Common Problems of Neurology. Indications for lumbar puncture. Instructor T. J. C. von Storch. J. Robert Shaughnessy, *Chairman*

BRISTOL SOUTH EAST

Tuesday December 12, at 4:00 p.m. at the Melrose Hospital Melrose. Syphilis in Pregnancy and the Offspring. Instructor Rudolph Jacoby. Walter H. Flanders, *Chairman*

BRISTOL SOUTH NORTH

Friday December 15 at 4:45 p.m., at St. John's Hospital Lowell. Syphilis in Pregnancy and the Offspring. Instructor C. Guy Lane. William S. Lawler, *Chairman*

WORCESTER (Milford Section)

Tuesday December 12 at 8:30 p.m., in the Nurses Home of the Milford Hospital Milford. Head and Spine Injuries. Instructor Walter R. Wegner. Joseph Ashkins, *Chairman*

WORCESTER (Worcester Section)

Friday December 15 at 8:00 p.m., in the Staff Room of the Worcester City Hospital Worcester. Con- vulsions in Infants and Children. Etiology and treatment. Instructor R. Cannon Eley. George C. Tully, *Chairman*

WORCESTER NORTH

Friday December 15 at 4:30 p.m. in the Nurses Home of the Burbank Hospital Fitchburg. Operative Deliveries. Instructor Roy J. Heffernan. George P. Keaveny, *Chairman*

DEATHS

BORDEN—CHARLES R. C. BORDEN M.D., of Brookline died November 28. He was in his sixty-sixth year. Born in Fall River he received his degree from Bowdoin Medical School in 1896. He was a staff member of the Boston City Hospital for about twenty years. Dr. Borden was consulting surgeon at the Brookline Contagious Hospital as well as at other local hospitals. For several years he was an instructor of otology at Harvard Medical School. In 1930 he retired from active practice.

Dr. Borden was a member of the Massachusetts Medical Society and the American Medical Association. He also held memberships in the American Laryngological, Rhinological and Otolological Society, the American Otolological Society, the New England Otolological and Laryngological Society and the American College of Surgeons.

His widow and a sister survive him.

CARROLL—JOHN J. CARROLL, M.D. of Holyoke died November 19. He was in his sixty-second year.

Born in Worcester he attended the local schools and in 1905 received his degree from the University of Maryland School of Medicine and College of Physicians and Surgeons.

Dr. Carroll had practiced in Holyoke for thirty-five years, thirty-two of which he served as city bacteriologist. He was a fellow of the Massachusetts Medical Society and the American Medical Association, and a member of the Holyoke Tuberculosis Society.

His widow and a daughter survive him.

DEXTER—SMITH O. DEXTER, JR. M.D., of New York City died November 25. He was in his thirty-third year.

He attended Harvard University and received his degree from Harvard Medical School in 1933. After serving his internship for two years at the Boston City Hospital he became associated with the Hygiene Department at Harvard. He was appointed a teaching fellow in medicine at Harvard Medical School in 1936 and later an assistant in medicine. At the time of his death he was assistant resident in medical research at the Rockefeller Institute in New York City where he had been associated for the past year.

Among his affiliations he held fellowships in the Massachusetts Medical Society and the American Medical Association.

SALLES—JOHN M. SALLES, M.D. of New Bedford, died November 26. He was in his fifty-sixth year.

Born in New Bedford he attended the local public schools and in 1911 received his degree from the Baltimore Medical College. He began practice the following year. Dr. Salles was senior physician of the staff of St. Luke's Hospital and served as physician at the Bristol County House of Correction. For many years he was a member of the Board of Health.

He was a fellow of the Massachusetts Medical Society and the American Medical Association, and a member of the New Bedford Medical Society.

A sister and a brother survive him.

CORRESPONDENCE

INAUGURATION OF A HEALTH-SERVICE PLAN IN MASSACHUSETTS

To the Editor: The inauguration of a budgeted health service plan in Massachusetts is probably of interest to

more physicians than the small number who have become associated with it at its inception. We believe, therefore, that the presentation of a brief description of the plan through the *Journal* is desirable. To this end we have prepared and are enclosing such a description, which we hope you will be able to publish.

As members of the Massachusetts Medical Society who have undertaken the task of organizing the medical service under the plan, we have gone to particular pains to protect the rights of the profession and the quality of the service rendered to the subscribers.

If the profession signifies its interest in further details of the plan, we shall gladly send you for publication, when you so desire, the various agreements pertaining to its organization and operation.

CHANNING FROTHINGHAM,
ROBERT L. DeNORMANDIE,
ALLAN M. BUTLER,
HUGH CABOT,
EDWARD L. YOUNG

* * *

Because of the increasing cost of good medical care, many individuals today, who are self-supporting in the absence of sickness, are forced to become charity patients when confronted with serious illness. Consequently, charitable services are subjected to an un contemplated burden and physicians are asked to provide free medical care to persons who should pay for professional services. This unsatisfactory state of affairs is recognized by charitable institutions, physicians and patients.

It is generally agreed that the most practical way to keep these patients medically self-supporting is to enable them to budget their medical expenses. The costs of illness are thereby distributed and largely paid for when they are well and when their earning power is not curtailed. Medical service plans to this end have been devised and set in operation by commercial insurance companies, consumer groups, professional groups, and county and state medical societies.

The cash indemnity plans offered by various insurance companies have not met the need. The strict eligibility requirements, the many exclusion-of-benefit clauses and the cancelability of these policies have limited their value. Consumer groups have too often suffered from want of professional knowledge concerning the problems involved and hence from the selection of inadequately qualified professional personnel. Professional groups have often operated on such a restricted basis that sound actuarial risks were not obtained. Most of the plans based on a unit system of payment for services rendered by all licensed physicians within the area covered have thus far proved so unsuited to efficient and economical operation that unsatisfactory service to patients or inadequate remuneration to physicians has been the result.

On the other hand, efficiently organized prepayment plans have been operated for many years by industrial groups, educational institutions and groups of physicians. Some of these plans call for compulsory payments. Others are on a voluntary basis. When well organized they have been able to provide good medical care to the subscribers and satisfactory remuneration to the physicians.

Believing that the consumers of medical care in Massachusetts should be given the opportunity of voluntarily budgeting professional medical costs, as they may voluntarily budget hospital charges, a group of physicians has agreed to furnish medical care to members of a prepayment health service made available by a charitable organization. Two considerations have been in mind in planning for the provision of this medical care. First, the service should make maximum use of and cause minimum

disturbance to existing private medical practice. Second, the service should be organized in the interests of efficiency and economy so that physicians may be adequately remunerated for services rendered without necessitating a charge to the subscribing members that would prevent voluntary enrollment. This second consideration obviously places certain limitations on wholly satisfying the first consideration. Yet, it is difficult to see how limitations essential to efficiency and economy are to be avoided if the service is to be financially sound and if physicians and patients are to be treated fairly. Fortunately, when fully analyzed, these limitations are not such as to warrant abandoning hope of extending voluntarily budgeted services, which provide a high quality of medical care and are financially sound.

The health service, which will become available to the public in March, may be outlined as follows. Health Service, Incorporated, has been chartered as a charitable corporation under Chapter 180 of the General Laws of Massachusetts, for the purpose, among others, "of establishing, maintaining and operating a nonprofit health plan whereby medical care and service, both preventive and curative, may be provided at low cost by individuals who are legally qualified to give such medical care and services with whom this corporation shall have contracts directly or indirectly for such care and services to such of the public of low income, resident in said commonwealth, as become subscribers to the plan and make monthly or other regular payments in accordance therewith." The establishment of a health service by a charitable form of corporation seems desirable for many reasons, among which are the following:

1. The service will be subject to the same public supervision as is that of all charitable corporations.
2. Recent court decisions have held that it is legally valid for charitable corporations to offer such a medical service.
3. It makes possible representation of the lay public, the subscribing members and the medical profession on the board of directors and in the management of the plan.

Members of Health Service, Incorporated, will consist only of individuals and their dependents whose family income is less than \$3500 a year. It will accept members only in groups in a manner somewhat similar to the acceptance of members by the Blue Cross. It furthermore recommends that its members be subscribers to a hospital service plan. Health Service, Incorporated, offers to its members professional medical service in the home, in the doctor's office and in the hospital.

A nonprofit partnership of physicians, known as Medical and Surgical Associates, will provide the medical service to the members of Health Service, Incorporated. In the furnishing of medical care, the relation of Medical and Surgical Associates to Health Service, Incorporated, is to be "that of an independent contractor, and Health Service, Incorporated, its officers and employees shall have no voice or authority in the manner, methods or details of the furnishing of said medical care." Physicians, therefore, will manage the medical aspects of the service, and yet will be relieved of the burden of offering the service or collecting the dues. The medical service provided to members by Medical and Surgical Associates will not only include care by practicing internists and pediatricians, but also the services of competent consultants and specialists of all kinds—obstetricians, surgeons, roentgenologists, ophthalmologists, otolaryngologists, bronchoscopists, cardiologists, dermatologists, anesthesiologists, and so forth. There will be no financial transactions between patient and physician. The patient will make all payments to the central office of

Health Service, Incorporated. The latter will turn over to Medical and Surgical Associates not less than 80 per cent of the payments received. From moneys thus available Medical and Surgical Associates periodically will make payments to physicians of the proportionate amounts to which they shall be entitled. There will be no fee schedule which will compete with or undersell existing medical fees. Any net profits shall be added to a reserve fund as required for the sound conduct of the business or shall be used to increase the income available to physicians rendering the medical care or to decrease the cost of medical care to the subscribing members. No profits will be distributable to the partners.

The opportunity thus offered for budgeting medical costs should permit many individuals in the low income group who are now forced to become medically indigent to remain the private patients of doctors. Should this prove to be the case, and should the doctors in the communities where members of this service live, co-operate with Medical and Surgical Associates in providing the medical care, the provision of this service to the public should cause little disturbance to existing private practice. To attain this aim co-operation with the profession is earnestly sought. Constructive criticism by the profession is eagerly desired.

The physicians participating in this medical partnership believe that the formation of such medical-service groups, organized in the interest of economy and efficiency for the provision of good medical care, should prove a conservative way of meeting many of the medical problems confronting us today. This plan and others like it should enable many people to obtain adequate medical care by budgeted payments which they can afford. It should diminish public dissatisfaction with medical services and lessen medical indigency. In so far as these ends are realized, the demand for compulsory health insurance should be lessened and the medical needs of the community more wisely satisfied.

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor In addition to the articles enumerated in our letter of October 14 the following have been accepted

Allen Laboratories, Inc.
Medipax Brand of Vaginal Tampon-Suppositories
With Merthiolate 1 2000
Medipax Brand of Vaginal Tampon-Suppositories
With Metaphen 1 2000

Gane's Chemical Works Inc.
Racophedrine
Racophedrine Sulfate

Wm. S. Merrell Company
Ampule Bismuth Subsalicylate in Oil 0.13 gm.
(2 gr.) 1 cc.
Ampule Mercury Salicylate in Oil 0.065 gm (1 gr.)
1 cc.
Ampule Mercury Salicylate in Oil 0.1 gm (1½ gr.)
1 cc.

National Drug Co.
Antimeningococcal Serum, Refined and Concentrated

E. R. Squibb & Sons

Amniotin-Squibb
Amniotin in Oil, 2000 international units
Amniotin in Oil, 10,000 international units
Amniotin in Oil, 20,000 international units
Amniotin Capsules, 1000 international units
Amniotin Capsules, 2000 international units
Amniotin Capsules, 4000 international units
Amniotin Pessaries, 1000 international units
Amniotin Pessaries, 2000 international units

Winthrop Chemical Co., Inc.
Luminal-Sodium Tablets, 1 gr

The following product has been accepted for inclusion in the List of Articles and Brands Accepted by the Council But Not Described in N.N.R."

Smith-Dorsey Co.
Tablets Ferrous Sulfate 3 gr

PAUL NICHOLAS LEECH Secretary

535 North Dearborn Street,
Chicago, Illinois.

VACANCIES IN 101ST MEDICAL REGIMENT

To the Editor Information from Washington indicates that additional units to complete the organization of the 101st Medical Regiment will be authorized in the immediate future. This will mean the organization of one hospital company one collecting company and three battalion headquarters. In all there are potential openings for about fourteen medical officers. Candidates for these commissions must be graduates of Class A medical schools, be registered by the Massachusetts Board of Registration in Medicine, be able to pass the required physical examinations, be able to qualify before the Massachusetts Military Service Commission and preferably be between twenty five and thirty four years of age. Officers of the regiment will gladly discuss the functions of the regiment and give detailed information relative to duties pay and allowances to prospective candidates or other interested physicians Tuesday or Friday nights from 8-00 until 10-00 at the South Armory Irvington Street, Boston.

KARL R. BAKER Colonel M. C.
Massachusetts National Guard
Commanding

South Armory
Irvington Street, Boston

REPORTS OF MEETINGS

WILLIAM HARVEY SOCIETY

On November 3, at the Beth Israel Hospital there was a meeting of the William Harvey Society of Tufts College Medical School. Dr. H. E. McMahon introduced the speaker Dr. Shields Warren whose subject was "The Effect of Radium and X-ray Irradiation of Tissues."

Dr. Warren, in recalling that his first interest in the subject emanated from a realization of the unfavorable aspects of irradiation of the leukemias stressed that the danger of these helpful therapeutic agents was still a reality. Indeed such a threat would always lurk where the untoward effects of irradiation made their appearance only after a delay of days to years after the exposure of tissues. Some interesting and striking evidences of the possible ill-effects were demonstrated by cases in the speak-

er's experience. There was the hemangioma overtreated in infancy due to the innocent ruse of a mother who lived to see a carcinoma arise at the site of the atrophic scar when the boy was eighteen years old. More rapidly effective results were the extensive burns of the fingers in an orthopedic intern, whose surgical career was ended due to a failure of his superiors to warn him of the insidious dangers of the fluoroscope when improperly used. Other examples of the dynamic effects of radioactive substances were the cases of the watch-dial painters, whose slight exposure over a period of years resulted in aplastic anemias, leukemias and osteogenic sarcomas. Finally, Dr Warren showed a photomicrograph of a fibrosarcoma which had arisen in the stroma of an epidermoid carcinoma that was finally cured by small multiple doses of irradiation.

The speaker chose to confine his remarks to the effects of the gamma rays of radium and the usual range of therapeutic x-rays rather than to discuss the possibilities of newer developments, such as the cyclotron.

Dr Warren reminded his audience that irradiation follows the general laws of the electromagnetic spectrum in that the intensity of the effect is inversely proportional to the square of the distance from the source of the rays. The second universal law of physics followed by these agents is that the effect of the irradiation hinges on the amount of absorption by the tissues, and that consequently the more penetrating, shorter, high voltage rays cause less damage to intervening normal tissue.

The first effect of irradiation discussed was that on living cells. Such effects, it was pointed out, might result from a direct action on the cells themselves, or as a result of changes in the connective-tissue stroma, or secondary to changes in the vascular supply. The picture seen in irradiated cells showed no qualitative difference when gamma rays of radium or various wave-lengths of x-rays were employed, showing that the essential effect of all rays in practical use was identical. In the cell, the first change noted was in the Golgi apparatus, which was broken up and heaped into a conglomerate mass. Later was seen a failure of the chromosomes to separate properly and an inability of the cells to carry on normal regeneration. Even in those cells able to reproduce, a loss of chromosomes resulted invariably in death of some of their progeny. It has become an accepted fact that cells in mitosis are far more pregnable to irradiation, especially when in the prophase. These phenomena were represented as the result of the absorption of radiant energy by the cell nucleus, the energy being produced by the ionization secondary to the impingement of high-velocity rays on the molecules. The changes described, however, were not held to be specific for irradiation, since heat, protoplasmic poisons and ultra violet light can produce such a picture. It is only when the entire tissue, with its characteristic cellular, stromal and vascular variations is considered that a specific irradiation effect is recognized.

Dr Warren also showed illustrations of the vascular changes induced by therapeutic x-rays and emphasized their importance in altering the nutrition of the irradiated area. It is the vascular endothelium which is particularly susceptible, and radiation therapy results in the formation of hyaline thrombi and a replacement of endothelium by connective tissue.

The importance of the substrate of a tumor in determining the outcome of irradiation therapy was illustrated by the comparison between a basal-cell carcinoma of the cheek and a similar lesion on the nose or ear. Due to the response of vascular and connective tissue, the results in the former region far surpass those in the latter areas where the lesions overlie bone or cartilage.

Dr Warren then proceeded to some of the more practical aspects of therapeutic irradiation. He showed how a clear understanding of the aforementioned inverse square law had allowed the clinicians to raise the curability rate of basal-cell carcinoma by removing the source of energy to such a distance that the entire tumor, and not merely the surface cells, received an adequate dosage. The insertion of seeds was another method described to attain proper distribution and adequate dosage of irradiation—two factors of far more importance than the type of irradiation employed.

The next topic discussed was the variation in sensitivity of tissues, the very fact which makes irradiation of therapeutic value. The well known sensitivity of the more immature and more undifferentiated cells was demonstrated by rabbit experiments and human results. Radium placed near one surface of a rabbit's ear caused after eighteen months a denuding of the epithelium of both surfaces without altering the differentiated, non-vascular intervening cartilage. In practical therapeutics Dr Warren pointed out the radio-resistance of gastrointestinal mucosa and its tumors compared with those of both alimentary orifices. Then again, radium treatment for cancer of the uterine cervix was shown by photomicrography to destroy entirely the cervical epithelial tumor cells while sparing the more highly differentiated glands of the endocervix.

The fact that even normal tissue had a considerable effect from irradiation was often overlooked with resultant ill effects in surrounding organs. The use of multiple portals focused on such a site as the cervix was considered the main answer to that problem. The use of small doses over a long period, unless properly spaced, does not solve the issue, for cells definitely acquire a tolerance on repeated irradiation, by whatever mechanism. One should plan to cure on the first attempt since recurrences are more radioresistant.

Dr Warren discussed some of the inevitable sequelae of even properly conceived therapy with these agents. Radiation burns were considered equivalent to surgical scars, making it necessary to consider such natural results in weighing the value of the therapy. Another of the more important side effects of irradiating biological material was the lowered resistance to infection which so often was discovered on subsequent ill advised surgery, such as a simple exodontia as long as two years after therapy had been terminated. The mechanism of this altered resistance was not a reflection of any measurable change in opsonic index, leukocytes or any other general factor. It seemed purely an unexplained localized interference with the normal protective powers.

In conclusion, Dr Warren mentioned some of the unsettled problems in the field of irradiation—the reasons for sensitivity and resistance which will explain how 200 r may control a lymphoma while 8000 r may have no effect on a sarcoma, the reason irradiation arrests mitosis primarily in the prophase while another agent arresting mitosis, colchicine, interferes largely at the metaphase, and the reason for the vacuolization of irradiated cells. The great promise of irradiation in the future of tumor therapy lies, thinks Dr Warren, in its almost phenomenal selectivity in regard to its lethal effect on tissues.

HARVARD MEDICAL SOCIETY

The season's first meeting of the Harvard Medical Society, held at the Peter Bent Brigham Hospital on October 10, 1939, was inaugurated with the customary presentation of cases.

The first patient was a twenty-three year-old man who

referred to the hospital by his local physician because of multiple infections of the fingers and toes. Five weeks before entry the patient "broke out with two carbuncles on his neck, which he treated with Sypho Naphol. He noted that these cleared up in about one week. One week later a carbuncle appeared over the spine of the right scapula, which was treated unsuccessfully by his local physician. Two weeks before admission the patient experienced what seemed to him a "cold," with a temperature of 101° F., a rough throat, a running nose and malaise. The illness had continued to date. Five days before entering hospital, the patient was awakened from sleep by throbbing pains in both third toes, thumbs and middle fingers. The use of Freezone resulted in severe blisters which were treated by excision and heat. When improvement was seen, the patient was referred to the hospital.

During the preceding month there had been nose bleeds on two occasions and dyspnea without exertion at times. There had also been one or two chills and night sweats. Four weeks before admission there had been blurring of vision of the left eye, and one week before admission a keratic tint was noted in the sclerae. There had been a weight loss of 15 pounds in the four week period. Physical examination revealed a pale, chronically ill man. There was questionable atrophy of the left leg. A granulating area 5 cm. in diameter was found on the spine of the right scapula, and a similar area on the spine over the left iliac crest. The lesions of the fingers and toes presented grayish sloughing macerated with multiple sinuses exuding a moderate amount of yellow fluid.

Laboratory findings revealed a moderate secondary anemia, a leukocytosis of 14,000 to 19,000 and a positive culture for *Staphylococcus aureus*. Urinalysis showed varying numbers of red and white blood cells. Examination showed osteomyelitis of both index fingers, but no infected bone was demonstrable elsewhere. The patient in the hospital had consisted of incision and drainage of the localized digital lesions, transfusions of whole blood, intradermal toxoid every second day and supportive measures. An autogenous vaccine was prepared.

The patient continued to have a temperature swinging between 100 to 104° F., while the local lesions showed only improvement. The impression on admission was that the case was one of furunculosis complicated by a moderate chemical burns and secondary infection.

Elliott C. Cutler in discussing the case cited the possibility of infection with a bacterium which is common in low virulence in a host who has a low immunity. He suggested that such a case might be an indication for the use of immunotransfusions as worked out by Jane Smith. Dr. Soma Weiss emphasized the importance of watchfulness for new metastatic abscesses, which should be drained immediately to lessen the chance of forming foci of infection.

The second case was that of a sixty-one-year-old man who had entered the hospital for the second time, having been in for increasing attacks of paroxysmal angina associated with ankle edema. On his first entry into the hospital previously the patient had had evidence of heart failure with precordial pain, rapid pulse and poor heart action. A basal metabolic rate at that time was greatly reduced, and a diagnosis of thyrotoxic heart disease was made despite the absence of a palpable gland. The diagnosis was not accepted and no operation was performed. At a time later however a subtotal thyroidectomy was performed at another hospital and the patient experienced gradually increasing relief from his painful cardiac

attacks. He felt essentially well until a few months before his second admission when he had had episodes of dyspnea without exertion but had experienced no pain.

In discussing the case, Dr. Samuel A. Levine pointed out the trend in acceptance of thyrotoxic heart disease as a true entity. The diagnosis of masked hyperthyroidism was not widely accepted ten years ago. He emphasized that the patient's complaint at the present admission was paroxysmal dyspnea rather than precordial pain relieved by nitroglycerin as on previous entry. Whereas before he had had heart disease he was now showing evidence of heart failure unassociated with any thyrotoxic element. Dr. Weiss continued the discussion with the pertinent reminder that anginal attacks usually disappear with the onset of congestive heart failure.

Dr. Cutler in introducing the speaker of the evening retraced the relatively short history of cardiac surgery from the first suture of a lacerated human heart in 1896 through the more recent attempts of Beck, Shaugnessy and others to improve the blood supply of impoverished myocardium by muscle and omental transplants. The speaker of the evening was Dr. Mercier Fauteux of McGill University and the Royal Victoria Hospital, Montreal and his subject was entitled "A New Surgical Method to Improve the Blood Supply to the Heart in Coronary Disease."

Dr. Fauteux's approach to the problem, although based on the pathology and pathologic physiology of coronary heart disease, differed from that of Beck and Shaugnessy in that he employed no external source to improve the blood supply to the heart. In order to determine the most commonly affected coronary artery the speaker examined two hundred hearts and corroborated the finding of Dr. Alan R. Moritz, formerly of Cleveland, that the left descending branch was wholly or partially occluded alone in 46 per cent of cases and in combination in another 25 to 30 per cent. It was therefore decided to limit experimental work to this commonly affected member of the coronary system.

Dr. Fauteux divided the disorders following coronary occlusion into a mechanical or hydraulic one and a physiologic one of vasoconstriction. Sympathectomy in angina pectoris was described as an attempt to alleviate spasm and pain by attacking the latter whereas the use of supplementary transplants was aimed at the mechanical inadequacy.

The pathological and physiological basis for the work of Dr. Fauteux was divided into two parts corresponding to the mechanical and physiologic disorders previously mentioned. The speaker himself had noted a fall in blood pressure distal to the occlusion of the ramus descendens. Consequently the small amount of arterial blood from the anastomotic bed was quickly drained by veins accustomed to a much greater blood volume and there was not enough time allowed for nourishment of the myocardium. The ligation of the coronary vein corresponding to the diseased artery seemed to be a logical procedure. This principle has been used in peripheral vascular disease with good results in some instances. As long ago as 1913 Appell reported the successful use of femoral vein ligation for gangrene of the toes. Makins, during the World War, advocated ligation of the corresponding vein when ever the artery to an extremity had to be sacrificed. Brooks also demonstrated the value of vein ligation. More recently Van Gorder has reported on the same successful results in gangrene of an extremity by ligation of the vein to the part. The mechanism suggested by the speaker to account for the phenomenon was that ligation of the vein increased the venous pressure which subsequently raised

the resistance of the capillary bed and caused its permanent dilatation. As a result the small flow from the anastomotic vessels became functionally valuable due to its slower and more widespread dispersion. Backflow from the venous side was not considered an important contribution. Acute experiments, that is, the ligation of a healthy artery and vein, showed the blood poorly aerated, but this could not be considered comparable to the conditions obtaining in coronary occlusion in man, where a gradual increase of anastomoses has been occurring while the main artery has been decreasing in caliber.

In order to prove his contention, Dr Fauteux tried to produce coronary occlusion by ligation of the descending branch of the left coronary artery at varying levels from its origin. In all instances, however, the dogs died immediately or within forty-eight hours from ventricular fibrillation. The speaker said he is now attempting to thrombose the artery gradually in order to simulate human coronary disease and then do a subsequent resection of the vessel. However, if the left coronary vein was first ligated and then the artery acutely occluded as in the above experiment, all the animals lived. When the animals were finally sacrificed, no gross changes were found in the myocardium and microscopic examination showed that normal vessels coursed through the small infarcts that were present. And so the mechanical insufficiency could be combated by ligation of the coronary vein.

In regard to the physiological problem of vasoconstriction, the speaker and others had shown that this phenomenon, although found in the presence of a diseased artery, was abolished when the affected artery was resected. In fact an actual dilatation followed such a procedure and an increased vascular supply to the area resulted. Therefore arteriectomy as well as ligation of the corresponding vein was the procedure followed in the experimental work on dogs, and the results were those reported above.

After four years of diligent investigation, Dr Fauteux believed that the results justified attempting the alleviation of coronary disease in man by a similar procedure. However, due to the technical difficulties of separating the coronary artery, resection of the artery was not to be attempted, but merely ligation of the left coronary vein. In April, 1939, a man with a history and electrocardiographic findings typical of coronary disease was operated on with comparative technical ease. An electrocardiogram two days after operation showed the formerly inverted T wave to be upright and other abnormalities to be decreased. Whereas formerly the patient could neither walk nor work, he was able within a few months to walk twenty-five minutes twice a day, resume light work and even gain weight with apparent impunity. Electrocardiographic studies during the operation showed no arrhythmias or pulse rate changes. Dr Fauteux emphasized the fallacy of drawing any general conclusions from one case and also the necessity of choosing future cases wisely. The patient must be evaluated and be known to have true coronary occlusion rather than a mild angina, and must be otherwise in excellent condition.

Dr Cutler initiated the discussion by suggesting that although the theory was sound where the injured artery was in the neighborhood of a rich anastomotic bed, such a state was not shown to exist in the myocardium.

Dr Weiss agreed with the speaker that the mechanism whereby the venous ligation benefited the myocardial nourishment was one of increased capillary resistance and increased capillary volume but made the further suggestion that as a result the same blood flow nourished more adequately due to the greater volume available. He suggested the analogy to chronic anemia, where a hemoglobin value of 20 to 25 per cent may sustain a person with com-

parative comfort, whereas one of 50 per cent in acute blood loss may be totally inadequate.

Dr Monroe J Schlesinger suggested that the tying of the artery immediately following that of the vein might merely take advantage of a temporary venous engorgement and that an interval should be allowed for equilibrium to occur.

Dr Fauteux replied that such an experiment had been done, ligation of the artery having been carried out one year after occlusion of the vein. The results in such a case proved even more striking, so that temporary congestion certainly was not the only or even the most important explanation.

Dr Robert E Gross was invited by Dr Cutler to report on his experiences with surgical attempts to increase the blood supply to the heart. Originally, the plan had been to cause adhesions between the pericardium and myocardium, but it was found that the vascularity was insufficient to offset any measurable ischemia. However, combination of adhesions and ligation of the coronary vein, as suggested by Dr Fauteux, has resulted in strikingly better vascularity. Dr Gross raised one objection to the procedure of venous ligation in the human being, namely that the proximity of the artery and vein might result in irritation of the artery with subsequent spasm and fibrillation in an already embarrassed heart.

Dr Fauteux suggested that the technical difficulties were not by any means insurmountable, and that the use of quinidine and novocaine solution as suggested by Beck and Moritz assured a lack of spasm and could even cause the heart to regain its regularity in experimentally produced arrhythmias.

In closing, Dr Cutler agreed with the speaker that the heart was in reality a tough organism which could stand considerable operative handling with minimal dysfunction, and that the technicalities were actually an insignificant difficulty. The outstanding problem would be a proper evaluation of the results obtained in a disease with so few measurable criteria. The meeting closed with the showing of a two-reel motion picture, explaining the rationale and showing the technical details of Dr Fauteux's animal experiments.

NOTICES

REMOVAL

JOHN R BARKER, M.D., announces the removal of his office to 1101 Beacon Street, Brookline.

BOSTON DISPENSARY

A luncheon meeting of the clinical staff of the Boston Dispensary will be held on Friday, December 15, in the auditorium of the Joseph H Pratt Diagnostic Hospital at 12 o'clock noon.

The program, under the auspices of the Social Service Department, will begin at 12:30 p.m.

Medical Social Service in the Boston Dispensary, 1908-1939

Its Beginning Mrs Hilbert F Day

Its Function Miss Kate McMahon

Report of the Year 1938 Miss Edith Canterbury

All interested in the subject are cordially invited to attend.

ROBERT W BUCK, M.D., *President*,
JAMES M BATY, M.D., *Secretary*

STON CITY HOSPITAL

The monthly clinicopathological conference will be held at the Boston City Hospital on Wednesday, December 13 12 o'clock noon in the Pathological Amphitheater

JOSEPH L. HALLISEY M.D. *Secretary*
Medical Staff

STON LYING IN HOSPITAL

There will be a meeting at the Boston Lying in Hospital on December 20 at 8 15 p.m.

PROGRAM

Delayed Labor Dr S A Cosgrove medical director
Margaret Hague Maternity Hospital Jersey City
New Jersey

STON DOCTORS' MPHONY ORCHESTRA



The Boston Doctors' Symphony Orchestra will rehearse under Alexander Theide former concert master with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, every Sunday at 8.30 p.m., in Studio A Station WMEX Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr Julius Loman Ham Hall Hotel Brookline (BEA 2430)

TUMOR CLINIC, BOSTON DISPENSARY

Each Tuesday and Friday morning 10 00 to 12.30 there is a meeting of the Tumor Clinic of the Boston Dispensary, a unit of the New England Medical Center. Neoplasms of various sorts are seen and discussed and when there is an indication are treated with radium or high-voltage x-ray. Physicians are invited to visit this clinic. They may bring patients for aid in diagnosis or may refer patients to the clinic following which a report will be rendered to the referring physician. A limited number of beds are available for diagnostic study and for treatment.

SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday December 19 at 12 o'clock noon. Dr John D Adams will speak on "Observations of Thirty Years' Experience in the Treatment of Fractures."

Physicians are cordially invited to attend.

JOHN B. HALL, M.D. *Secretary*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday December 12 at the amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance) at 8 15 p.m.

PROGRAM

Presentation of cases
Tissue Electrolytes. Dr A Baird Hastings.
Medical students and physicians are cordially invited to attend.

ROBERT M ZOLLINGER, M.D., *Secretary*

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday December 13 from 2 to 4 p.m. Drs. John Homans and S A. Levine will speak on "Edema." A clinicopathological conference conducted by Dr Elliott C. Cutler will take place from 4 to 5 p.m.

On Thursday December 14 from 8.30 to 9.30 a.m. there will be at the Children's Hospital, a combined clinic, conducted by Dr Frank Ober of the medical, surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER, M.D., *Secretary*

CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the Carney Hospital will be held on Monday December 11 at 11 30 a.m.

PROGRAM

Case reports.
Urinary Incontinence in the Female The Kennedy operation (with lantern slides and demonstration)
Dr R. J. Heffernan. Discussion Drs. L. E. Phaneuf R. C. Graves and E. L. Kickham.

Physicians and medical students are cordially invited to attend.

ROY J. HEFFERNAN M.D., *Secretary*

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held at the Peter Bent Brigham Hospital Monday December 18 at 8 15 p.m.

PROGRAM

Nature of the Peripheral Resistance. Drs. E. A. Stead, Jr., and Paul Kunkel
The Hemodynamic Effects of the Application of Tourniquets Dr R. V. Ebert
Constructing Pleuritis and Pericarditis. Drs. C. S. Burwell and G. D. Ayer
Uncommon Types of Heart Disease. Dr Soma Weiss.
Is the Ewart's Sign due to Pericardial Effusion? Dr F. C. Gevalt, Jr.
The Value of Electrocardiography in the Prognosis of Coronary Thrombosis. Dr F. F. Rosenbaum
Sulfamidamide and Heparin in the Treatment of Subacute Bacterial Endocarditis. Drs. P. B. Beeson and S. A. Levine

Interested physicians and medical students are invited to attend.

EDWARD F. BLAND, M.D., *Secretary*

NEW ENGLAND ROENTGEN RAY SOCIETY

The next meeting of the New England Roentgen Ray Society will be held on Friday December 15 at 8 p.m. at the Beth Israel Hospital

PROGRAM

Roentgen Visualization of the Coronary Arteries. Dr M. J. Schlesinger
Clinical Implication of the Pathologic Findings. Dr H. L. Blumgart.
The Value of Cholangiography During Operation. Dr C. G. Mixer

Early Diagnosis of Prepyloric Carcinoma Dr Karl Presser
 Changes in the Uterus Following Roentgen Therapy Demonstrated by uterography Dr W S Altman.
 Observations on Contact Roentgen Therapy Dr H. F. Friedman

Dinner at the Harvard Club will be served at 6 30 p.m.

LANGDON P. THAXTER, M.D., *President*,
 AUBREY O. HAMPTON, M.D., *Secretary*

NEW ENGLAND DERMATOLOGICAL SOCIETY

The next meeting of the New England Dermatological Society will be held on Wednesday, December 13, at 2 00 p.m. at the Boston City Hospital

BERNARD APPEL, M.D., *Secretary*

UNITED STATES MARINE HOSPITAL

The staff meeting of the United States Marine Hospital, Chelsea, Massachusetts, will be held at 'The Hut,' on Friday afternoon, December 15, at 4 00

PROGRAM

Handwriting and Personality Mr John C. G. Loring

JOHN W. TRASK, *Medical Director in Charge*

PHI DELTA EPSILON

The Phi Delta Epsilon medical fraternity will hold its thirty sixth annual convention at the Waldorf Astoria Hotel on December 29 and 30. About 600 physicians and medical students from this country and Canada will attend. Dr Morris Fishbein, editor of the *Journal of the American Medical Association*, who is national president of the fraternity, will preside at the sessions.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, DECEMBER 11

MONDAY DECEMBER 11

- *11 30 a.m. Carney Hospital Monthly clinical meeting and luncheon
- *12 15 p.m.-1 15 p.m. Clinicopathological conference Dr S. Burt Wolbach Peter Bent Brigham Hospital amphitheater

TUESDAY DECEMBER 12

- 9-10 a.m. Some Ophthalmoscopic Signs in Constitutional Disease Dr Joseph J. Skirball Joseph H. Pratt Diagnostic Hospital
- 10 a.m.-12 30 p.m. Boston Dispensary tumor clinic
- *12 15 p.m.-1 15 p.m. X-ray conference Dr Merrill C. Sosman Peter Bent Brigham Hospital amphitheater
- 8 15 p.m. Harvard Medical Society Amphitheater Peter Bent Brigham Hospital (Shattuck Street entrance)

WEDNESDAY DECEMBER 13

- *9-10 a.m. Hospital case presentation Dr S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital
- *12 m. Clinicopathological conference Children's Hospital amphitheater
- 12 m. Boston City Hospital Monthly clinicopathological conference. Pathological amphitheater
- 2 p.m. New England Dermatological Society Boston City Hospital
- 2 p.m.-4 p.m. Joint medical and surgical clinic Peter Bent Brigham Hospital

THURSDAY DECEMBER 14

- *8.30 a.m.-9.30 a.m. Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital at the Children's Hospital
- 9-10 a.m. Gastrointestinal clinic Presentation of cases Dr K. S. Andrews Joseph H. Pratt Diagnostic Hospital

FRIDAY DECEMBER 15

- *9-10 a.m. Sir James Mackenzie General practitioner Dr Joseph H. Pratt Joseph H. Pratt Diagnostic Hospital

- *10 a.m.-12 30 p.m. Boston Dispensary tumor clinic
- *12 m. Urological conference at the Massachusetts General Hospital lower amphitheater Out Patient Department
- 12 m. Clinical meeting of the Children's Medical Service, Massachusetts General Hospital Ether Dome
- *12 m. Boston Dispensary Clinical staff meeting Auditorium of the Joseph H. Pratt Diagnostic Hospital
- 8 p.m. New England Roentgen Ray Society Beth Israel Hospital

SATURDAY DECEMBER 16

- *9-10 a.m. Hospital case presentation Dr S. J. Thannhauser Joseph H. Pratt Diagnostic Hospital
- *10 a.m.-12 m. Medical staff rounds of the Peter Bent Brigham Hospital Conducted by Dr Marshall N. Fulton

*Open to the medical profession

- DECEMBER 8 — William Harvey Society Page 676 Issue of October 26.
- DECEMBER 8 — Waltham Hospital Staff meeting Page 880 issue of November 30
- DECEMBER 11 — Carney Hospital Monthly clinical meeting and luncheon Page 917
- DECEMBER 12 — Harvard Medical Society Page 917
- DECEMBER 13 — International College of Surgeons Page 880 issue of November 30
- DECEMBER 13 — Boston City Hospital Monthly clinicopathological conference Page 917
- DECEMBER 13 — New England Dermatological Society Notice above.
- DECEMBER 13 — Peter Bent Brigham Hospital Joint medical and surgical clinic Page 917
- DECEMBER 14 — Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital Page 917
- DECEMBER 14 — Pentucket Association of Physicians 8 30 p.m. Hotel Bartlett Haverhill
- DECEMBER 15 — New England Roentgen Ray Society Page 917
- DECEMBER 15 — Waltham Hospital Clinicopathological conference. Page 880 issue of November 30
- DECEMBER 15 — Boston Dispensary Clinical staff meeting Page 916
- DECEMBER 15 — United States Marine Hospital Notice above.
- DECEMBER 18 — New England Heart Association Page 917
- DECEMBER 19 — South End Medical Club Page 917
- DECEMBER 20 — Boston Lying in Hospital Page 917
- DECEMBER 22 — Waltham Medical Club Page 880 issue of November 30.
- DECEMBER 27 — Metropolitan State Hospital Clinicopathological conference. Page 880 issue of November 30
- DECEMBER 29 and 30 — Phi Delta Epsilon Notice above
- JANUARY 6 JUNE 8-11 1940 — American Board of Obstetrics and Gynecology Page 160 issue of July 27 and page 798 issue of November 16.
- JANUARY 22-25 1940 — American Academy of Orthopaedic Surgeons Hotel Statler Boston
- FEBRUARY 11-14 — International College of Surgeons Page 759, issue of November 9
- MARCH 2 JUNE 8 and 10 — American Board of Ophthalmology Page 719 issue of November 2
- MARCH 7-9 1940 — The New England Hospital Association Hotel Statler Boston
- MAY 14 1940 — Pharmacopoeial Convention Page 894 issue of May 25
- JUNE 7-9 1940 — American Board of Obstetrics and Gynecology Page 1019 issue of June 15

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 3 1940 — Semi annual meeting Combined meeting with Essex South Danvers State Hospital, Hathorne 7 p.m.

ESSEX SOUTH

JANUARY 3 1940 — Head Injuries Dr John S. Hodgson. Danvers State Hospital Hathorne.

FEBRUARY 14 — Cough Sputum Hemoptysis — How shall they be investigated? Dr Reeve H. Betts Essex Sanatorium Middleton

MARCH 6 — Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections Dr Champ Lynn Lynn Hospital Lynn

APRIL 3 — Addison Gilbert Hospital Gloucester

MAY 8 — Annual meeting Salem Country Club Peabody

HAMPSHIRE

JANUARY 10 1940

MARCH 13

MAY 8

All meetings are held at 11:30 a.m. at the Cooley Dickinson Hospital Northampton

MIDDLESEX EAST

JANUARY 10, 1940

MARCH 20

MAY 15

Meetings are held at 12 15 p.m. at the Unicorn Country Club Stoughton

MIDDLESEX NORTH

JANUARY 31, 1940.
JUNE 24.
JULY 31
OCTOBER 30.

SOMERSET SOUTH

DECEMBER 7
JANUARY 4 1940
FEBRUARY 1.
MARCH 7
APRIL 4
MAY 2.

All meetings, with the exception of one which is usually held at the Quaker City Hospital are held at the Norfolk County Hospital in South Braintree, at 12 o'clock noon.

PLYMOUTH

JANUARY 18, 1940—Brookline Hospital, Brookline.
MARCH 21—Goodwill Hospital, Brookline.
APRIL 18—St. Ann's.
MAY 16—Lakeville Sanatorium, Lakeville.

BUTOLK

JANUARY 31, 1940—Scientific meeting. Subject to be announced later.
MARCH 27—Scientific meeting. Symposium on Ulcerative Colitis and Dermatitis. Under the direction of Dr. Chester M. Jones.
APRIL 24—Annual meeting in conjunction with the Boston Medical Society. Election of officers. Program and speakers to be announced later.

WORCESTER

DECEMBER 13—St. Vincent Hospital.
JANUARY 10 1940—Worcester City Hospital.
FEBRUARY 14—Worcester State Hospital.
MARCH 13—Worcester Memorial Hospital.
APRIL 10—Worcester Massachusetts Hospital.
MAY 8—Worcester County Club.
Each meeting begins with dinner at 6:30 p.m. and is followed by a program and scientific meeting.

BOOKS RECEIVED FOR REVIEW

Obstetrical Manikin Practice Lyle G. McNeile. 111 pp. Baltimore: Williams & Wilkins Co., 1939. \$2.00.

Electrocardiographic Patterns Their diagnostic and clinical significance Arlie R. Barnes. 197 pp. Springfield, Illinois and Baltimore: Charles C. Thomas, 1939. \$3.00.

Proctoscopic Examination and Diagnosis and Treatment of Diarrheas M. H. Streicher. 149 pp. Springfield, Illinois, and Baltimore: Charles C. Thomas, 1940. \$3.00.

The Essentials of Medical Treatment David M. Lyon. 48 pp. Edinburgh and London: Oliver & Boyd, 1939. \$1.

A Mirror for Surgeons Selected readings in surgery Arce Power. 230 pp. Boston: Little, Brown & Co., 1939. \$2.00.

Liquor The servant of man Walton H. Smith and Ferdinand C. Helwig. 273 pp. Boston: Little, Brown & Co., 1939. \$2.00.

The Hospital Care of Neurosurgical Patients Wallace Hamby. 118 pp. Springfield, Illinois and Baltimore: Charles C. Thomas, 1940. \$2.00.

Human Helminthology A manual for physicians, sanitarians and medical zoologists Ernest C. Faust. Second edition. 780 pp. Philadelphia: Lea & Febiger, 1939. \$5.00.

The Electrocardiogram and X-Ray Configuration of the heart Arthur M. Master. 222 pp. Philadelphia: Lea & Febiger, 1939. \$6.50.

Endocrine Gynecology E. C. Hamblen. 453 pp. Springfield, Illinois, and Baltimore: Charles C. Thomas, 1939. \$5.50.

The Surgery of Injury and Plastic Repair Samuel Fernon. 1409 pp. Baltimore: Williams & Wilkins Co., 1939. \$15.00.

Principles and Practice of Aviation Medicine Harry G. Armstrong. 496 pp. Baltimore: Williams & Wilkins Co., 1939. \$6.50.

BOOK REVIEWS

Proctology for the General Practitioner Frederick C. Smith. 386 pp. Philadelphia: F. A. Davis Co., 1939. \$4.50.

This book appears to be of uncertain value. Doubtless the medical student or general practitioner would find profitable information. Much of the material is well presented, and the advice as to treatment is for the most part correct and authoritative. The arrangement of the subject matter however is such that there is much unnecessary repetition. The first two chapters, for instance, could be omitted without detriment because practically every thing included therein is re-stated in the chapters dealing with the specific disease conditions. The book would likewise be improved and perhaps more likely to be read if the rather sketchy chapters on pilonidal cysts, intestinal parasites, constipation, diarrhea and surgery of the colon were omitted. These subjects hardly belong in a book on proctology and have been much better described in other books.

In addition one must mention several statements which it would seem are incorrect, misleading or at least controversial. For example, it is painful to the surgical "aseptic conscience" to have an author advise the performance of rectal examinations without protecting the finger with a glove or finger cot. There must be few well informed surgeons who believe that in general spinal anesthesia is just as safe as ether. How many anesthesiologists would agree that the anesthetic combination of nitrous oxide and oxygen with ether does not present danger of explosion when used in the presence of a cautery? What is one to suppose is meant by the "dorsal prone" position? Who also believes nowadays that the so-called nutrient enemata are of distinct alimentative value? The reviewer furthermore objects vehemently to the frequent use of the term "division of the sphincter" which has been warned against by several generations of surgeons. The author must intend the reader to translate this to the proper word, "dilatation." Furthermore one cannot agree that the treatment of anal cancer is always radiological. It takes little experience with the use of radium or x-ray in this region to learn that radical surgical excision gives better results and makes patients more comfortable. It would seem to have been wise too, to avoid the controversial subject of the role of the so-called "diplosteptococcus" of Barger as the cause of ulcerative colitis. It is unfortunate also to have a present-day author group the operations of ileostomy and colectomy together as surgical treatment and call them both unsatisfactory every well-informed surgical intern knows better. But it would take another book to point out all the defects. One is left with the impression however that the book should have been confined to the subject of proctology.

The Harvey Lectures Delivered under the auspices of the Harvey Society of New York 1938-1939 Series XXIV 279 pp. Baltimore: The Williams & Wilkins Co., 1939. \$4.00.

It is with considerable eagerness that we look forward to the collected Harvey Lectures which are issued yearly by the Harvey Society. They are the "salt" of medical progress in specialized fields. This year's impressive array of lectures deserves special reference: Marnett, "Some Aspects of the Intermediary Metabolism of the Steroid Hor-

mones", Wcech, "The Significance of the Albumin Fraction of Serum", Du Bois, "Heat Loss from the Human Body", Colin, "Proteins as Chemical Substances and as Biological Components", Park, "Observations on the Pathology of Rickets with Particular Reference to the Changes at the Cartilage-Shaft Junctions of the Growing Bones", Linderstrom-Lang, "Distribution of Enzymes in Tissue and Cells", Danforth, "Genic and Hormonal Factors in Some Biological Processes", Szent Gyorgyi, "Biological Oxidation and Vitamins". The reviewer is not a sufficient authority in any of these fields to make any critical remarks. The text can be recommended to anyone interested in the foregoing subjects.

John Howard (1726-1790), Hospital and Prison Reformer. A bibliography. Leona Baumgartner. 79 pp. Baltimore. The Johns Hopkins Press, 1939. \$1.00.

Mr. Arnold M. Muirhead, whose own collection of Howardiana is now in the library of Dr. John F. Fulton, of Yale University School of Medicine, in his introduction to this book writes: "Here, at last, collected from many scattered sources, is presented in one volume with scholarly orderliness, and yet also with human interest, all the available bibliographical information about John Howard—an inestimable service for which collectors and students alike will long be grateful."

This book will become an indispensable part of the intellectual equipment of those who are or may be interested in prison reform, the public health movement and the history of medicine. Such readers will always be indebted to Dr. Leona Baumgartner for her efforts in this direction.

Symposium on the Synapse. Herbert S. Gasser, Joseph Erlanger, Detlev W. Bronk, Rafael L. De Nô, and Alexander Forbes. 474 pp. Springfield, Illinois, and Baltimore. Charles C. Thomas, 1939. \$2.00.

This symposium on the mechanism of synaptic transmission, held under the auspices of the American Physiological Society, has been reprinted from the *Journal of Neurophysiology*.

The five contributors and their subjects are: Herbert S. Gasser, "Axons as Examples of Nervous Tissue"; Joseph Erlanger, "The Initiation of Impulses in Axons"; Detlev W. Bronk, "Synaptic Mechanisms in Sympathetic Ganglia"; Rafael L. De Nô, "Transmission of Impulses through Cranial Motor Nuclei"; and Alexander Forbes, "Problems of Synaptic Function."

This brochure contains a most stimulating discussion of the chemical versus the electrical theories of synaptic transmission. The important point as to whether acetylcholine is a specific product released with regularity at the ganglionic synapses during the act of nerve transmission is re-examined. While the problem cannot at present be stated in precise terms, each student interested in the function of the nervous system will place this volume in a distinct place on the shelves of his library.

District Health Development. Building program as related to the master plan for the City of New York. Department of Health, City of New York. 53 pp. New York. Neighborhood Health Development, Inc., 1939. \$1.00.

This is an account of the present state of the building program of the Department of Health of New York City, together with sufficient explanation to emphasize the imperative need of decentralized administration for the largest city's health program. A loose-leaf planographic

process is employed, giving very readable typewriting and good illustrations.

The central unit consists of headquarters and a laboratory in Manhattan. Of an approximate total of thirty district health-center buildings, a half are either completed or under construction. In addition a score or more substations are proposed. Budgets and architects' plans are included.

Tuberculosis and Social Conditions in England. With special reference to young adults. P. D'Arcy Hart and G. Payling Wright. 165 pp. London. National Association for the Prevention of Tuberculosis. 1939. 3s.

It is essential in a discussion of the results of this study that reference be made to a similar survey on young women carried out in this country by Edna Nicholson and published in 1938 by the National Tuberculosis Association.

After careful consideration of several apparent etiologic factors in tuberculosis, the American study draws the following conclusion: "We believe, although it cannot be statistically proved, that psychic and physical changes of adolescence and early adult life cause young women to be unusually susceptible to tuberculosis and are the fundamental reason for the high mortality rate." The English workers, too, agree that young women are especially sensitive, probably on a biological basis, to tuberculosis, but they add that such individuals are also very susceptible to environmental factors.

Both studies agree that changes in personal habits, such as the hours spent in bed, the hours of work, the adequacy of meals, clothes, or the money spent on luxuries, have little significance. However, in regard to changes in living standards, such as housing, increasing employment of young women, and poverty, there is no agreement. The English authors stress the fact that the diminution in decline of deaths due to pulmonary tuberculosis is primarily associated with a diminution in rise of standard of living which occurred at the turn of the century.

As a standard of living, the authors used three yardsticks: the incidence of persons receiving poor relief; Stock's Social Index—the proportion of males in the lower economic grades; and the incidence of substandard housing—more than two persons per room. The incidence of tuberculosis was highest among those with poor housing conditions and among those on poor relief. The authors contend that the statistics for housing serve not only as an index for poverty as a whole, but also as a measure of comparing the degree of personal contact. They further add that the apparent improvement in mortality rates since 1933 may possibly be due to an increase in the building of new houses, with its effect on overcrowding.

While the American study by Miss Nicholson concludes that the lessened decline of mortality among young women is entirely due to the female biological factors, the English authors find that it may also be due to the effect of industrial occupation during the important years of adolescence and early adulthood, as well as the decline in the rise of living standards accompanied by setbacks in the improvement of housing conditions.

The English study is very thorough and in all respects seems to be superior to the one done in this country. The sources and methods used by the authors are above reproach, and care has been taken to account for possible sources of error. This study should be of great interest to all persons interested in the epidemiological and social aspects of pulmonary tuberculosis.

The New England Journal of Medicine

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VOLUME 221

DECEMBER 14, 1939

NUMBER 24

RIBOFLAVIN DEFICIENCY IN MAN*

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NEW YORK CITY

SINCE 1933 we have observed in 15 patients the characteristic skin and mucous membrane lesions now believed to be a manifestation of riboflavin deficiency. At first we thought that these lesions were uncommon manifestations of pellagra. After Sebrell and Butler¹ had experimentally produced similar lesions in human beings and cured them with synthetic riboflavin we recognized and proved the true nature of the condition.

Riboflavin, the accepted² name for vitamin B₂, described³ chemically as 6, 7-dimethyl-9-(d-1'-xyl)-isoalloxazin, is a necessary constituent in the diet of many animals. In the rat its lack leads to a failure in growth, senility, alopecia, a non-specific dermatitis and cataract formation in the eye. An acute deficiency⁴ leads to spasticity, generalized weakness, circulatory collapse and a "yellow" liver, while a chronic partial deficiency⁵ results in signs characterized clinically by ataxia although riboflavin is presumably present in every living cell and is concerned with the chemical reactions involved in cell respiration,⁶ no distinct clinical syndrome in man had been attributed to its deficiency prior to Sebrell and Butler's¹ report.

The lesions produced by Sebrell and Butler in 10 of 18 women maintained on the diet of Goldberger and Tanner⁷ appeared ninety-four to one hundred and thirty days after the beginning of the experiment. They began

as a pallor of the mucosa of the lip in the angles of the mouth without involvement of the buccal mucosa.

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This diet consisted of cornmeal, grits, wheat flour, rice, sweet potatoes, eggs, collards, fat pork, lard, cane syrup, sugar and vitamin-free cream.

This pallor was soon followed by maceration and within a few days superficial transverse fissures appeared, usually bilateral and exactly in the angle of the mouth. These fissures extended somewhat downward from the angle. In some instances the fissures continued to extend onto the skin for a distance of as much as half an inch. These lesions resemble those described as *perlèche*. At about the time the fissures were seen, the lips became abnormally red along the line of closure. This was due apparently to a superficial denudation of the mucosa. In addition to the cheilosis there was also seen a fine, scaly, slightly greasy desquamation on a mildly erythematous base in the nasolabial folds on the alae nasi in the vestibule of the nose and on the ears.

Under the conditions of the experiment these lesions were alleviated by the administration of synthetic riboflavin, but not by nicotinic acid. The authors' conclusion that the condition is a manifestation of riboflavin deficiency seems warranted. Since then, Oden, Oden and Sebrell⁸ have reported 3 patients from rural Georgia with similar lesions which responded promptly to 5 mg. of synthetic riboflavin given daily. They believe, since the Odens have seen many similar cases in their practice in rural Georgia that ariboflavinosis is in all probability a common deficiency disease in the southern United States. Sydenstricker⁹ thinks that these lesions are "even more frequent than frank pellagra."

The first patient in whom we recorded the occurrence of these lesions presented such a unique dermatosis that in subsequent cases such lesions were designated by his name. Fifteen patients with similar lesions have been observed: 6 men, from thirty to thirty-eight years of age, and 9 women, from twenty-five to fifty. Thirteen were alcohol addicts, 1 had advanced pulmonary and intestinal tuberculosis and 1 was an epileptic. In addition to riboflavin deficiency 5 patients had pellagra, 5 pellagra and polyneuritis, 1 pellagra polyneuritis and scurvy, 2 pellagra and scurvy and 1 polyneuritis, 1 patient showed no manifesta-

tions of other deficiency disease. The series therefore includes 13 cases of pellagra, 7 of polyneuritis and 3 of scurvy. The facial lesions seen consisted of filiform excrescences of a seborrheic nature, apparently derived from the sebaceous glands and varying in length up to 1 mm., closely to sparsely scattered over the skin of the face. Their characteristic location was in the nasolabial folds, but in addition they occurred frequently on the alae nasi, occasionally on the bridge of the nose and sometimes on the forehead above the eyebrows. The skin on which the excrescences were located was the seat of a fine, scaly, greasy desquamation. On casual inspection these filiform lesions resembled urea frost, but they could not be brushed off by rubbing with the fingers. In addition most of the patients showed fissures and maceration at the angles of the mouth, and a degenerative, crust-like formation on the epithelium of the lips, most marked on the lower. The fissures at the angles of the mouth were bilateral and extended laterally 1 to 3 mm. onto the mucous membrane of the mouth and 1 to 10 mm. onto the skin. They were usually very shallow but were sometimes 0.5 mm. deep, and their bases as a rule showed little or no increased redness. Extending for 5 to 20 mm. from the angle of the mouth onto both lips, the mucous membrane was macerated and wrinkled and pearl-gray. The lips, particularly the lower, frequently showed a marked increase in the vertical fissuring, often without a break in the mucous membrane. Occasionally the vestibule of the nose was involved, with lesions similar to those on the lips. We observed no lesions on the ears.

Our first 10 subjects, all of whom were pellagrins, were maintained on the diet of Goldberger and Tanner. After a control period of three to fifteen days, during which neither the facial lesions nor the cheilosis improved, various preparations then being tested for their value in the treatment of pellagra were given. Preparations which produced a cure of the stomatitis of pellagra were followed also by disappearance of the facial and lip lesions now ascribed to riboflavin deficiency.* These were Vegex, brewers' yeast and liver residue. Highly concentrated liver extract effective in pernicious anemia, cod-liver oil, linseed oil, cevitamic acid and thiamin chloride were ineffective not only in pellagrous stomatitis but also on these facial and lip lesions. For this reason we believed that the lesions were all part of pellagra. The following case report, in addition to describing the first case in which these distinctive

lesions were recognized, is fairly representative of the 10 cases in which the lesions responded to Vegex, brewers' yeast or liver residue.

CASE 1 L. P., a 35 year-old, white, alcoholic vagabond, was admitted to the Medical Service of the Psychiatric Division of Bellevue Hospital on June 25, 1933, complaining of a sore mouth, diarrhea and dermatitis. He had been drinking heavily and eating little and irregularly for at least 3 months. Mentally he presented a Korsakoff psychosis. Physically he had a pellagrous dermatitis of the hands, stomatitis, glossitis, diarrhea, normocytic anemia and peripheral neuritis. He was maintained on a diet poor in the vitamin B complex plus cod-liver oil, after 1 week he was given in addition, by parenteral injection, a concentrated liver fraction effective in pernicious anemia, 9 cc. daily for 7 days, and thereafter 3 cc. daily. This was followed by slight improvement in the dermatitis of the hands and in the anemia, but at the end of 42 days no improvement was noted in the glossitis, stomatitis, diarrhea or peripheral neuritis. At this time we observed an unusual lesion on the patient's face. It consisted of fine filiform seborrheic excrescences about 0.5 mm. in length, distributed in the nasolabial folds, on the alae nasi, on the bridge of the nose and on the forehead above the eyebrows. The liver extract was discontinued and the patient was thereafter maintained on the same diet, plus 18 gm. of Vegex by mouth daily. Within a week the glossitis, stomatitis and diarrhea disappeared and the peripheral neuritis and dermatitis of the hands improved, it was not until the 18th day of this regimen, however, that a significant improvement was noted in the lesions about the nose and forehead. From this time on the facial lesions rapidly improved, so that by the 34th day of treatment they had completely disappeared. The Korsakoff psychosis remained, however, and the patient was committed to a state hospital for the insane.

The appearance of the facial lesion while the patient was under observation and being maintained on a diet poor in the vitamin B complex, the failure of cod-liver oil to prevent its development and its cure following the addition of Vegex to the same diet led us to believe that it was a manifestation of deficiency in some fraction of the vitamin B complex. Since the recognized pellagrous lesions of stomatitis, diarrhea and dermatitis were simultaneously though more rapidly cured, we believed that this lesion was one of the less common manifestations of pellagra.

The results in this case were confirmed in 9 subsequent cases which showed the same distinctive lesions. When, however, we began the treatment of our pellagrins with nicotinic acid while still maintaining them on the diet poor in the vitamin B complex, although we obtained dramatic responses in the oral, gastrointestinal and mental manifestations of pellagra, the facial and lip lesions were not affected. After the response to nicotinic acid, 2 of these patients were given a full diet supplemented with 18 gm. of Vegex daily by mouth. The characteristic facial and lip le-

*The synthetic riboflavin, thiamin chloride and cevitamic acid used in this study were supplied by Merck and Co., Rahway, N. J.; the nicotinic acid by Merck and Co. and by the S.M.A. Corporation, Chicago; the Vegex and brewers' yeast by Vegex, Inc., New York City; the liver residue by Lederle Laboratories, Inc., New York City.

ons promptly responded. The following case illustrative.

CASE 2. D. G., a 31 year-old, unemployed, alcoholic Negro, was admitted to the Medical Service of the Psychiatric Division on December 8 1938 complaining of anorexia and fatigue of many weeks duration and a sore tongue and mouth of 1 week's duration. He gave a history of drinking at least 1½ pints of whisky daily for many years about 4 weeks before admission he had increased his whisky intake and reduced his food consumption to practically nothing.

Physical examination revealed the following significant findings. There was a nystagmus on lateral gaze. The patient had difficulty in opening his mouth because of pain. The tongue was scarlet red and the papillae were almost completely absent. The buccal mucous membrane was markedly reddened. In addition there were a few small,



FIGURE 1. Patient D. G. (before treatment)

filiform, pearl-gray ulcerations on the buccal mucous membrane opposite the molar teeth and on the floor of the mouth. At the angles of the mouth there were fissures and maceration (Fig. 1). The lower lip showed cracking and degeneration of the superficial epithelium. Across the bridge of the nose and in the nasolabial folds, extending to the cheeks and less so across the forehead, were greasy yellow excrescences. There was an acute balanitis, the prepuce being identical with that of the mucous membrane of the mouth. A mild peripheral neuritis was present, but there was no dermatitis of the hands, feet, perineum or neck.

The patient was maintained on the diet poor in the vitamin B complex. On the 6th hospital day the stomatitis and balanitis were worse. The filiform lesions in the nasolabial folds and the fissures and maceration at the angles of the mouth were unchanged. For the next 4 days, ten capsules of 100 mg. of nicotinic acid were given daily by mouth. Improvement in the stomatitis and balanitis was noted within 24 hours. By the end of the 4th day of nicotinic acid therapy (10th hospital day) the oral and penile lesions had completely healed. The fissures and maceration at the angles of the mouth and the filiform dermatitis, however, were unchanged, and the peripheral neuritis became worse. The patient was then given a vitamin B diet, plus 18 gm. of Vegex by mouth and 20 mg. of cyanocobalamin chloride by intramuscular injection daily.

The peripheral neuritis improved and in 14 days the filiform excrescences and the fissures and maceration had disappeared.

While this patient was on the ward, but after the regimen of the vitamin-rich diet with the supplements had been started, Sebrell and Butler's¹ report appeared. Their description of the lesions which they had produced experimentally suggested to us that the lesions we had been observing in our subjects were probably signs of more advanced states of riboflavin deficiency. If true, this observation would explain their failure to respond to nicotinic acid and their response to a full diet plus Vegex, brewers' yeast or liver residue, substances rich in riboflavin. We therefore determined to test the effect of synthetic riboflavin on the lesions occurring in our subjects. Since then we have observed 3 more such patients, 2 women and 1 man. Two of these cases are reported in detail. The third patient, a young Negroess with widespread pulmonary and gastrointestinal tuberculosis who had a typical nasolabial filiform dermatitis and lip lesions, died of tuberculosis before the effect of the treatment with riboflavin could be demonstrated.

CASE 3. J. B., a 45-year-old alcoholic Negro painter was admitted to the Medical Service of the Psychiatric Division on March 24 1939 complaining of soreness of the



FIGURE 2. Patient J. B. (before treatment)

mouth and throat, soreness in the vestibule of the nose, a "breaking out of the skin" weakness and difficulty in walking for 1 month. He gave a history of long indulgence in whisky up to the onset of the symptoms. During the previous few months he had eaten little and irregularly meat, milk, eggs and vegetables being excluded from his diet. After the onset of the symptoms he had discontinued alcohol and subsisted on soup.

Physical examination revealed the following significant findings. There was a bilateral nystagmus on lateral gaze. The tongue (Fig. 2) was smooth and slightly fissured and moderately red, with ulcerations on the tip and frenulum covered with a pearl gray exudate. The oral mucous membranes showed abnormal redness. On the floor of the

mouth there were ulcerations and exudate similar to those on the tongue. The lower lip showed degeneration of the epithelium with crusting and scaling. There were fissures at the angles of the mouth extending about 5 mm from the angles onto the skin of the face. In this area there was considerable maceration and a grayish, moist slough, distinctly noticeable in Figure 2. The upper lip was normal except for a slight increase in the horizontal fissures. On both alae nasi (Figs 2 and 3), and especially prominent in the nasolabial folds, were heaped up, seborrheic excrescences consisting of tightly packed filiform projections

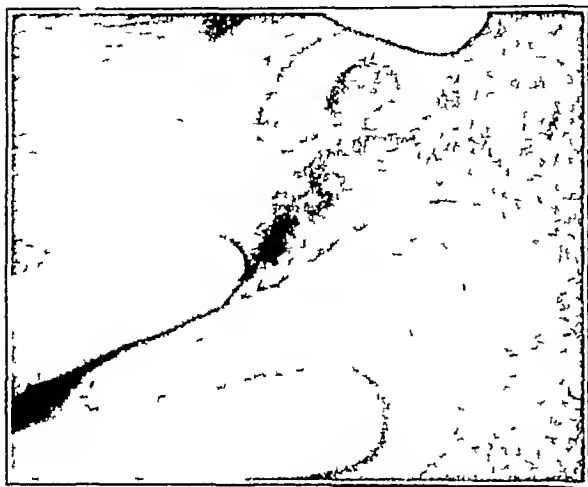


FIGURE 3 Patient J B (before treatment)

Inside the nares (Fig 3) was seen a crusted, elevated exudate not easily removable. Over both hands and elbows there was a dry, chronic, pellagrous lesion, and the skin of the groin and perineum was rough, pigmented and moderately reddened. There was no evidence of peripheral neuritis. Diagnoses of riboflavin deficiency and nicotinic acid deficiency were made.

Within an hour after admission the patient was seen by Dr W. H. Sebrell, who expressed the opinion that these lesions were those of riboflavin deficiency, more advanced than those produced by Sebrell and Butler experimentally.

The patient was maintained on the diet poor in the vitamin B complex, plus 200 cc. of 5 per cent glucose in physiologic saline solution, given by mouth every hour for the first 2 hospital days. On the 3rd and 4th days, without change of diet, he was given 50 mg. of synthetic riboflavin per day intramuscularly, and thereafter 10 mg. daily by mouth. By the 5th day definite improvement was noted in the fissures at the angles of the mouth (Fig 4), their depth was not so great and the maceration was almost healed. The lesions in the nasolabial folds and nares also showed a decrease in the degree of heaping up of the filiform excrescences, and the degeneration of the epithelium of the lower lip was much lessened. While these lesions were clearing, the oral lesions involving the tongue, floor of the mouth and buccal mucous membranes grew worse, with an increase in redness and ulcer formation, a moderately severe diarrhea also developed. It was deemed inadvisable to withhold nicotinic acid therapy for these pellagrous lesions. Continuing the same regimen, the patient was given in addition 1000 mg. of nicotinic acid per day orally in divided doses for 3 days. Rapid cessation of the diarrhea and healing of the dermatitis followed.

Meanwhile the nasolabial dermatitis and the lesions of the lips and angles of the mouth continued to improve.

On the 12th hospital day the patient developed signs of mild peripheral neuritis. This condition responded promptly to the administration of thiamin chloride in doses of 10 mg. per day intramuscularly for 3 days. On the 17th day the lesions in the nasolabial folds were almost entirely healed, only a small pigmented area without heaped up excrescences remaining. The deep fissuring at the angles of the mouth and between the nares and upper lip was healed and the epithelium of the lips was normal. The lesions in the perineum had entirely healed, and the old chronic pellagrous lesions of the hands and elbows were gradually clearing. From the 18th day the patient was given a diet rich in vitamin B, plus 18 gm. of Vegex daily, other supplements being discontinued. He was discharged on the 40th day.

CASE 4 V B, a 34-year-old, white woman, was transferred from an institution for the care of epileptics, where she had been a patient for the previous 5 years, to the Medical Service of the Psychiatric Division on January 28, 1939. She complained of weakness, bleeding gums, sore mouth and a rash on the face and hands of a few weeks' duration. The history included epileptic convulsions since the age of 3, a craniotomy in 1932 without improvement in the convulsions and an appendectomy in 1921. Her diet (as eaten by the patient) had consisted chiefly of the following: breakfast, oatmeal, coffee and white bread,



FIGURE 4 Patient J B (after five days of riboflavin therapy)

lunch, white bread and butter, potatoes and a portion of stew, supper, tea, white bread and butter, prunes and apricots. She received one egg per week. She never ate the meat in the stew but gave it to others. She consumed daily large amounts of cake furnished by her parents, so that the main constituents of her diet were cake and white bread.

Physical examination disclosed a thin, undernourished, well-oriented and co-operative woman. There was a bilateral nystagmus on lateral gaze. The lower lip showed degeneration, with scaling and desquamation of the epithelium. There were fissures at the angles of the mouth.

A seborrheic lesion consisting of filiform excrescences about 0.5 mm. in length appearing to protrude from the sebaceous glands, was present in the nasolabial folds and across the bridge of the nose. The lesion superficially resembled area frost but could not be rubbed off and the underlying skin felt greasy. It was not present on the upper lip, vestibule of the nose, forehead or ears. In addition there was an acneiform eruption over the face, which was so prominent as to hide most of the filiform lesions. The upper jaw was edentulous. The gums of the lower jaw were red and markedly piled with bags of blood around the teeth they bled at the slightest touch. The tongue was clean, bald and slightly reddened as were the mucous membranes. Along the frenulum a pearl-gray ulceration was present. On the right hand there was deep pigmentation over the second interphalangeal joint and thumb a small amount of ulceration over the knuckles and a bracelet-like, pigmented dermatitis of the wrist. The left hand exhibited a bracelet-like, pigmented dermatitis and a slight dermatitis over the second interphalangeal joint. There was increased keratosis of the elbows. There were no "necklace lesions" and no perineal lesions. There was no evidence of peripheral neuritis. Diagnoses of riboflavin, nicotinic acid and cevitamic acid deficiencies and epilepsy were made.

The patient was maintained on the diet poor in the vitamin B complex. Studies of the blood revealed total absence of cevitamic acid. The patient was given 300 mg. of cevitamic acid daily by intravenous injection and 100 mg. four times daily by mouth. On the 3rd hospital day there was definite improvement in the gums in that redness was decreased and they bled less readily on pressure. In the following day the gums were natural in color except for a small area adjacent to one of the incisors, which was still reddened but did not bleed. The dose of cevitamic acid was reduced to 200 mg. daily by mouth. The stomatitis and glossitis remained unchanged. From the 6th hospital day the patient was given 500 mg. of nicotinic acid daily in doses of 100 mg. by mouth. By the 8th hospital day the abnormal redness of the tongue and mucous membranes of the mouth had disappeared, the frenulum ulcer had healed and the dermatitis of the hands was clearing. The lesions on the face and lips, however, were unchanged.

At this time the patient was seen by Dr. V. P. Sydenhacker who expressed the opinion that the filiform lesions on the face and the lesions in the angles of the mouth and hands were due to riboflavin deficiency.

After 11 days of nicotinic acid therapy and the diet poor in the vitamin B complex there seemed to be no significant change in the filiform lesions on the face or the lip lesions. Beginning on the 17th hospital day administration of nicotinic acid was discontinued and 10 mg. of synthetic riboflavin was given daily by mouth. On the 5th day of this regimen a marked improvement was noted. The generative epithelial lesion of the lips and the fissures in the angles of the mouth had cleared entirely the filiform lesions on the nasolabial folds and the bridge of the nose had disappeared and the acneiform rash had improved. The patient, however, showed distinct signs and symptoms of mild peripheral neuritis. She was given 50 mg. of thiamin chloride daily by intramuscular injection. This was followed by complete disappearance of the signs and symptoms of peripheral neuritis within 3 days. From the 24th hospital day the patient was maintained with the regular ward diet, supplemented by 200 cc. of orange juice and 18 gm. of Vegex daily the administration of synthetic riboflavin, cevitamic acid and thiamin chloride being discontinued. The strength of the patient markedly improved,

and her weight, then 84 pounds had increased to 111 pounds when she was discharged on the 53rd hospital day.

These 2 cases proved that the filiform facial lesions and the lip lesions which we had previously noted could be cleared by Vegex, brewers' yeast or liver residue, but not by nicotinic acid, would heal on the administration of synthetic riboflavin. The response was obtained in 1 case before nicotinic acid was administered and while the signs of nicotinic acid deficiency were progressing in the other case the signs of nicotinic acid deficiency were first cured by nicotinic acid and subsequent administration of synthetic riboflavin cured the filiform dermatitis and the lip lesions.

DISCUSSION

We believe that the lesions described in this paper represent more advanced lesions of the same etiology as those experimentally produced and described by Sebrell and Butler.¹ The only difference is the presence of the filiform lesions in our subjects, but these occur on the same fine, scaly slightly greasy base, in the same distribution and associated with the same lip lesions as in the cases produced experimentally. Furthermore, the non-experimental lesions of our patients responded to the same therapeutic test as did the experimental lesions of Sebrell and Butler. Neither our lesions nor theirs were improved by nicotinic acid, both responded to riboflavin, whether given in its natural form² as contained in Vegex brewers' yeast or liver residue, or in its synthetic form.

It is interesting to note that 13 of our 15 patients showed in addition signs of nicotinic acid deficiency and 7 showed signs of thiamin deficiency. Spies and his associates³ reported 40 patients with riboflavin deficiency as manifested by lesions similar to those reported by Sebrell and Butler. About half their subjects also had pellagra. The coexistence of these deficiencies is not an unexpected phenomenon since these three vitamins are with a few exceptions distributed in the same foodstuffs. This suggests that in patients manifesting a clinical deficiency of any one vitamin other fractions of the vitamin B complex whether known or not as yet chemically identified or other accessory elements of nutrition may also be playing a role in the production of symptoms. This experience is illustrated in Case 4. In this case, scurvy was cured by cevitamic acid, pellagra was cured by nicotinic acid, filiform facial lesions and cheilosis were cured by synthetic riboflavin and polyneuritis, which developed while the patient was being maintained with the diet poor in the vitamin B complex, was cured by thiamin chloride. On the other hand, the patient failed to gain weight or strength and her

acne did not completely disappear until she was given a vitamin-rich diet supplemented with Vege.

It is probable, as Vilter, Vilter and Spies⁹ have suggested, that other manifestations hitherto considered a part of the pellagra syndrome are also due to riboflavin deficiency. Four endemic pellagrins maintained by them with a pellagra-producing diet and supplements of nicotinic acid and thiamin showed rapid improvement, but when continued on the same regimen these patients began to lose appetite and weight, and the investigators observed the appearance of what they described as a mild dermatitis. They then administered riboflavin to these patients and observed improvement within forty-eight hours, although the dermatitis appeared to be more chronic than the characteristic pellagrous dermatitis.

An interesting phenomenon in our cases of riboflavin deficiency was the preponderance of women over men. Nine (60 per cent) of our 15 patients with riboflavin deficiency were women, while only 26 per cent of the pellagrins routinely admitted to this service are women and the ratio of men to women admitted is 6:4. Spies and his associates⁹ have also seen this deficiency most frequently in women, and in all 3 cases reported by Oden, Oden and Sebrell⁶ the patients were women.

The nonexperimental cases of riboflavin deficiency in man seen by Oden, Oden and Sebrell⁶ and by Spies and his associates⁹ have occurred in the South, where pellagra is endemic. The fact that 10 cases were recorded by us in New York City before we recognized the true nature of the lesions, and the fact that since Sebrell and Butler's¹ report we have seen an average of 1 case per month on this service, while the average admissions were 272 per month, indicate however, that the disease may be not uncommon in the northeastern states. This seems to be more like-

ly in view of the now recognized frequency in this area of the lesions due to other fractions of the vitamin B complex, and the generally coincident distribution of those nutritional elements with riboflavin in foodstuffs.

SUMMARY AND CONCLUSIONS

We have described lesions in 15 patients which are similar to, though more advanced than, those produced experimentally by Sebrell and Butler. These lesions consist of filiform, seborrheic excrescences distributed most often in the nasolabial folds but frequently involving the alae nasi and less often the bridge of the nose and the forehead, superimposed on a skin which has a fine scaly, greasy desquamation in the same locations and cheilosis, characterized by maceration and fissures at the angles of the mouth and degeneration of the epithelium of the lips, especially the lower.

These lesions, like those produced experimentally, improve following the administration of natural or synthetic riboflavin, but fail to respond to diets poor in the vitamin B complex or to nicotinic acid. We therefore feel justified in attributing them to riboflavin deficiency.

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THE ETIOLOGY AND PATHOGENESIS OF THYROTOXICOSIS, WITH SPECIAL REFERENCE TO ITS PITUITARY ORIGIN*

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THE etiology and pathogenesis of thyrotoxicosis have an enormous literature, and continue to be subjects of considerable controversy. In considering the gradual alteration of opinions concerning these subjects, we should look on them from a double point of view, that is to say, intrinsic and extrinsic factors should be differentiated.

INTRINSIC FACTORS

The intrinsic abnormality of the thyroid gland which would cause thyrotoxicosis would be a condition in which the gland has primarily lost its ability to retain the elaborated hormone. Such a condition represents a sort of thyroid diarrhea, as Kochert called it, which permits, or occasions, an excessive escape of thyroid hormone into the blood stream. Indeed, Wilson and Kendall (1916) were the first to prove that the amount of thyroxine in the thyrotoxic gland is smaller by one-fifth or one twentieth than the amount in the normal thyroid gland. They interpreted it as a result of increased secretion into the circulation. This is in line with the increase in total blood iodine (Veil and Sturm, 1925; Lunde et al., 1929; Curtis et al., 1933) in direct relation with that of thyroxine (Elmer, Rychlik and Scheepers, 1934). The last-named writers found the thyroxine iodine level in blood to be elevated ranging from 8 to 5 micromg per 100 cc., while normally it varies between 3 and 5. Naturally the total blood iodine level is much greater. In agreement with this, Veil (1933) found the iodine elimination in urine and bile greater in patients with thyrotoxicosis than in normal individuals. Curtis and his associates (1934) and Scheffer (1937) went farther on this matter by determining the iodine elimination in the feces, by the skin and by the lungs, thus giving a more complete picture of the increased iodine excretion from a thyrotoxic body. These researches show in thyrotoxicosis a negative iodine balance which in severe cases must naturally lead to the depletion of iodine. It is not surprising that the clinical improvement which has been clear since the introduction of iodine

by Plummer and Boothby (1924) may be at least partly explained outside the inhibiting effect of iodine, by the covering of the increased loss in iodine.

In the secretion of the thyroid hormone, we meet at once the question raised by Moebius (1886), Plummer and others as to whether in thyrotoxicosis a normal or an altered hormone is secreted. The former hypothesis is based, on the one hand, on the relief of thyrotoxicosis produced by iodine treatment, suggesting that a less-iodized hormone is elaborated and on the other hand, on the much stronger effect of thyroglobulin obtained from thyrotoxic thyroid glands than of that from normal ones. Since Gaddum (1927-1930), Abderhalden and Wertheimer (1928) and Kendall (1931) have shown that thyroxine derivatives containing less iodine produce a much weaker effect than does thyroxine the first hypothesis of less-iodized hormone is no longer tenable.

With regard to the second possibility, that of secretion of an altered hormone, the great divergence of opinions should be emphasized. These opinions either favor the theory of dysthyroidism (F. Muller, 1927; Cooksey and Rosenblatt, 1928; Saito, 1933; Lerman and Salter, 1934) or undermine it by showing that biologic activity per unit of iodine is even too low in thyrotoxic glands (Krogh and Lindberg, 1932; Palmer and Leland, 1935). Thus the problem of dysthyroidism still remains to be elucidated.

An entirely different view was proposed by Abelin (1932) and later supported by Brugsch (1935). The outcome of Abelin's investigations was the conception that di-iodotyrosine is an anti-hormone of thyroxine. He suggested that in normal organisms there is an equilibrium between these two hormones, and that in thyrotoxicosis this equilibrium is disturbed by thyroxine's becoming predominant. This hypothesis was supported by the experiments carried out by Abelin and Wegelin (1932). They found that if guinea pigs were given the thyrotropic hormone intraperitoneally, the effect produced on the histological structure of the thyroid gland was reduced or even completely inhibited by simultaneous oral administration of di-iodotyrosine.

Our experiments might confirm Abelin's conclusion that di-iodotyrosine reduces the action of

*Presented at a meeting of the Harvard Medical Society, Boston, April 11, 1937.
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For listing of the references, the reader is referred to Dr. Elmer's book, *Diagnosis and Thyroid Function* (London: Oxford University Press, 1933).

thyrotropic hormone, nevertheless, they might also show that this inhibitory effect produced by inorganic iodine in equivalent dosage is as great as that of di-iodotyrosine, if not greater. Since inorganic iodine produces the same effect as di-iodotyrosine, the action produced by the latter cannot be regarded as specific. It seems that the inhibitory effect is due merely to iodine released by the breakdown of the di-iodotyrosine in the body. Abelin, however, argued that di-iodotyrosine does not break down in the body, and besides he suggested that the effect produced by potassium iodide is due to the iodine's being synthesized to di-iodotyrosine. In order to ascertain whether the decomposition of di-iodotyrosine takes place, I took 0.2 gm of di-iodotyrosine (116 mg of iodine) by mouth and found that it broke down rapidly, since inorganic iodine could be demonstrated in the urine in the first hour, and 57 mg of inorganic iodine, that is, half of the ingested di-iodotyrosine iodine, was recovered in the twenty-four-hour urine. It appears also from more recent experiments of Snapper and Grünbaum (1937) that the *o*-di-iodophenolic group is not responsible for the inhibitory effect on the thyroid gland, since *n*-benzoyl-di-iodotyrosine, which as is known does not break down in the body, has no influence on the condition of patients with thyrotoxicosis.

Thus it appears that there is no justification in accepting the hypothesis either of the existence of di-iodotyrosine as an antihormone of thyroxine, or of the disturbance in thyroxine-di-iodotyrosine equilibrium as a primary cause of thyrotoxicosis.

EXTRINSIC FACTORS

Most probably extrinsic factors play an important part in the etiology and pathogenesis of thyrotoxicosis. It is known that the thyroid gland is subordinated in its activity to the anterior pituitary, and possibly indirectly or directly to the nervous system, moreover, it is correlated with adrenal cortex, sex glands and liver.

The Role of the Adrenal Cortex

The experiments of Marine and his associates (1930) led them to advance the hypothesis that in thyrotoxicosis the fundamental disturbance is due to primary insufficiency of the adrenal cortex. The loss of the control over the oxidative processes occurring in deficiency of function in the suprarenal cortex might result in a physiologic attempt at compensation by an overproduction of thyroid hormone. This seemed to follow from the experiments of Marine and Baumann (1932), who found in rabbits and cats after sublethal injury of the adrenal cortex a transient complex of symptoms which closely resembled thyrotoxicosis. In

agreement with this, small suprarenals have usually been found in thyrotoxicosis by Marine (1930).

Now the question arises whether the activity of the adrenal cortex on the thyroid gland should be ascribed to the cortin, or to the cevitic acid, or to the vitamin B complex which is believed to be connected with the adrenal cortex. Marine and his associates attributed a marked significance both to the cortical hormone and to the cevitic acid. This claim is based on the one hand on the observation made by Marine and Shapiro (1921) that a rapid improvement after oral administration of fresh suprarenal cortex was observed, and on the other hand on the experiments carried out by Marine, Baumann and Rosen (1934) indicating that the cevitic acid partially inhibits the thyrotropic action of the anterior pituitary extract on the thyroid gland in guinea pigs. With regard to the latter experiments, we (Elmer, Giedosz and Scheps, 1935) can indeed confirm the partial inhibitory effect of cevitic acid in hyperthyroidism induced by thyrotropic injections in guinea pigs, but no inhibitory effect could be obtained by us (Elmer, Giedosz and Scheps, unpublished data) after treatment either with cortical extract or with synthetic cortin, desoxycorticosterone acetate. We do not wish, however, to deny that the adrenal glands may suffer from pathologic alterations in the course of thyrotoxicosis, and that some symptoms, for example lack of energy and muscle strength, may be due to the loss of the endocrine activity of the cortex. In such cases, of course, cortin may be beneficial in abolishing the above symptoms, but never those of thyrotoxicosis itself. The role of the cevitic acid seems to be rather a secondary one, owing to its depletion in the adrenal cortex, that is, in the greatest reservoir in the body.

Since the belief in the primary role of cortin and cevitic acid is hardly probable, it might be expected that the third constituent, riboflavin (Laszt and Verzar, 1935), believed to be essential for the function of the adrenal gland, plays some role in thyrotoxicosis. Some authors have suggested that riboflavin acts as an antagonist to the thyroid hormone (Kuhnau and Stepp, 1933), and that its lack is a fundamental factor in the development of thyrotoxicosis. Recently, Hoen and Oehme (1938) have found that vitamin B₂ in small doses prevents the enlargement of the adrenal cortex usually caused by injections of thyroxine.

We carried out experiments bearing on the relation between thyroid and riboflavin. In young guinea pigs treated simultaneously for a week by thyrotropic hormone in doses corresponding to 6 to 50 mg of dried anterior pituitary powder and

by 1 mg of crystalline riboflavin, we failed to find any traces of its inhibiting effect either on the hyperfunctioning thyroid gland or on the enlarged adrenal cortex. In view of our experiments, the role of riboflavin in the etiology of thyrotoxicosis should be questioned.

Since we are speaking of vitamins, I may be permitted to dwell briefly on vitamins B₁ and A. Some authors believe that thyrotoxicosis is caused either by hypovitaminosis, due either to a lack of vitamin B₁ (Kühnau and Stepp, 1933) or of vitamin A (Abelin, 1931). In view of the possible role of these vitamins, we (Elmer, Giedosz and Scheps, 1937) have studied the effect of crystalline vitamins B₁ and A on the hyperfunctioning glands of guinea pigs that had been treated by thyrotropic hormone. It seems to follow from our experiments that a close antagonism between the thyroid gland and vitamin B₁ is hardly possible, since we failed to see any inhibitory effect of vitamin B₁ on the gland.

Some authors have focused attention on vitamin A, regarding it as an antagonist to thyroxine (Abelin, 1931, H Euler and Klusman, 1932). Our own investigations (Elmer, Giedosz and Scheps, 1935) have shown that the administration of vitamin A, at least in huge doses, partly inhibits the action of the thyrotropic hormone on the thyroid gland. But the role of vitamin A appears to be rather secondary. It should be pointed out that the impairment of the liver caused by the thyroid overactivity occurs parallel with the reduction in its reserve supply of vitamin A, 95 per cent of which is normally stored in the liver.

In summary, it can be said that a more or less marked deficiency of the vitamins may appear at the onset of thyrotoxicosis. The hypovitaminoses result either from increased consumption to some extent proportional to the metabolic level or from reduced absorption of vitamins due to the disturbances in the alimentary canal (hypochlorhydria, diarrhea). It is therefore not surprising that the requirement of vitamins is increased in thyrotoxicosis, and their administration is justified in the treatment, but there seems to be no sufficient justification for accepting their primary role in the etiology of thyrotoxicosis. We agree with Means (1937) that vitamins, except perhaps vitamin A, have no marked, if any effect on the thyroid gland itself comparable with that of iodine.

The Role of the Gonads

There is no doubt that the normal relation between the ovaries and the thyroid gland is very close. This relation is displayed among other ways, by the quite important iodine content of the ovaries, by the influence of ovariectomy on the

iodine in the thyroid gland and blood and by the changes in iodine metabolism which occur at different functional periods of the ovaries, namely during menstruation and pregnancy and at the time of the menopause. In particular during the menopause, which is not rarely connected with the development of thyrotoxicosis, the blood iodine level is slightly increased (Jahn and Kesselkaul, 1928). In hypernodemia Cucco (1932) sees a manifestation of increased thyroid activity which seems to be confirmed by the depressing effect of ovarian extracts.

According to Levy-Simpson (1937) and Loeser (1938) both estrone and testosterone exert a beneficial effect in some cases of thyrotoxicosis, which might, in our opinion be attributed to the depressing effect on the pituitary gland rather than to direct action on the thyroid gland. This seems at least to follow from our recent experiments, in which no inhibitory action either of estrone or of testosterone could be demonstrated in guinea pigs injected with thyrotropic hormone (Elmer, Giedosz and Scheps, 1938).

Finally, it should be mentioned that the role of the ovaries must be considered more important than that of the testicles, since thyrotoxicosis appears three to six times more frequently in women than in men.

The Role of the Anterior Lobe of the Pituitary Gland

A new era was opened by Loeb in 1932 with the fundamental discovery of the thyrotropic hormone, and with the reproduction in guinea pigs of all the principal symptoms of Graves's disease. Loeb's insight has allowed him to put forward the bold hypothesis that the action of the anterior lobe is involved in the etiology of thyrotoxicosis, although it may be only one of several factors concerned in this condition. However, there was one serious objection to such a hypothesis, namely the fact, observed by Loeb himself and confirmed later by Collip and Anderson (1934) and many others, that the thyroid gland and the clinical picture of thyrotoxicosis return to their normal state in spite of the continuation of injections of thyrotropic hormone. The development of this resistance to thyrotropic activity raised the hypothesis of antihormones being normally present in the blood and counteracting the action of thyrotropic hormone (Collip and Anderson 1934). We shall not discuss here the great divergence of opinions in explanation of the development of the refractory state. It should be pointed out only that Loeser (1937) has shown that the refractoriness does not appear if continuously increasing

large doses of thyrotropic hormone are administered to guinea pigs

Attempts to overcome this difficulty and to produce maintained experimental hyperthyroidism have been made by us in dogs and guinea pigs (Elmer, Giedosz and Scheps, unpublished data). Five dogs varying between 4.5 and 65 kg in weight were treated with daily intravenous injections of thyrotropic hormone in continuously increasing doses, together with 0.15 to 2.0 gm of dried cattle anterior-pituitary powder per kilogram of body weight, for five or six weeks. In all 50 to 150 gm of anterior-pituitary powder was injected into a single dog. Six young guinea pigs weighing 180 to 200 gm were treated with thyrotropic hormone in increasing large doses for five or six weeks, during which time 55 to 75 gm of dried anterior-pituitary powder was used.

The thyrotropic hormone was prepared by us according to Loeb's acid method. In order to avoid some difficulties in injecting large volumes of pituitary extract, we concentrated it ten to twenty fold to a small volume by ultrafiltration at ice temperature, so that 1 cc of extract corresponded to 0.5 to 1.0 gm of anterior-pituitary powder.

We succeeded in obtaining maintained experimental hyperthyroidism in all dogs and guinea pigs. The thyrotoxic condition was manifested by nearly all signs of thyrotoxicosis: general weakness and nervousness, loss in weight, dehydration, polyuria, rise in temperature, marked heart symptoms, increase in basal metabolic rate, hyperiodemia, increased iodine excretion in the urine and hypocholesterolemia with disturbance in estrification. Other symptoms, such as nausea, vomiting, diarrhea and eye signs, were inconstant. All dogs died either during the treatment or seven to ten days after the last injection, having shown general weakness and severe loss in weight. The loss in weight was so great that even increased appetite could not compensate for it. This loss and the slight increase in temperature were probably due to the increased catabolism. Indeed, the basal metabolic rate was always markedly and continuously elevated.

The heart damage was unmistakably evidenced by electrocardiographic changes which should be looked on as specific to a thyrotoxic condition. These often began early, and were comparable in their typical form to those in human thyrotoxicosis. The commonest abnormalities in the electrocardiograms were increases in height of the R and P waves and in depth of S₃, an inversion of T₃ and sometimes the preponderance of the left ventricle. In some dogs only increased P and T waves, which furnish evidence of sym-

pathicotonia, were observed. This typical complex in the advanced course of thyrotropic treatment may change and pass into the electrocardiographic picture which is encountered in coronary insufficiency and sometimes complicates the long-standing onset of human thyrotoxicosis. In agreement with this, we found prominent alterations in the coronary vessels, evidenced by thickening of the walls and narrowing of the lumens. In most of the dogs the heart was enlarged, a phenomenon which was mainly due to hypertrophy of the left ventricle. Histologically there was myocardial damage, manifested by the degeneration of heart muscle (loss of striations and of uniform appearance).

The hypocholesterolemia was very prominent in the second period of the treatment, the value dropping to one third of the original level, that is, from 150 to 50 mg per 100 cc. The ratio of total cholesterol to cholesterol ester was markedly disturbed, dropping to 25 per cent (normally above 40 per cent), which is evidence of severe injury to the liver. Indeed, histologically the liver showed far-advanced changes: loss of uniform appearance, dissociation of cells and, frequently, fatty degeneration and fatty infiltration. Perhaps to the damaged liver function should be referred the terminal drop of blood sugar (from 110 to 65 mg per 100 cc). It should be remarked that liver glycogen was intensively mobilized (0.7 per cent). All this agrees closely with the hypocholesterolemia observed by Hurxthal (1933), and with the frequency of hepatic anatomic changes observed by Beaver and Pemberton (1933) and other authors in human thyrotoxicosis. So it is not surprising that Boothby regards hepatic lesions as an integral part of the syndrome of thyrotoxicosis.

But the most interesting changes were observed in the thyroid glands, which in all the animals appeared histologically to be hyperfunctioning, so that in some cases it was difficult to identify the gland. The histologic aspect falls into line with a high decrease in total iodine, which occurred chiefly at the expense of thyroxine iodine which decreased from 300 to 400 micromg per 100 cc to 40. It can safely be said that the thyroid glands were seriously depleted of thyroxine. A marked hyperiodemia, even to 60 micromg, and increased excretion of iodine in the urine, from 10 to 40 micromg daily, apply without doubt to this thyroxinorrhea, to which a rise in basal metabolic rate really corresponds.

With regard to other endocrine organs, it should be mentioned briefly that far-advanced changes were observed only in the gonads, particularly in the ovaries, which became highly atrophic, and in the anterior lobe of the pituitary gland, which was almost completely deprived of its acidophilic cells.

The disappearance of these cells seems to favor the view that they manufacture the thyrotropic hormone, and it may be regarded as a condition of atrophy from disuse, due to injections of the thyrotropic hormone.

The Role of the Nervous System

The interrelation between the thyroid and the anterior pituitary glands on the one hand and the nervous system on the other may be effected either by humoral (blood or lymph) or by nervous paths. Collin (1925) designated as *hémocrinie centrale* the connection between the pituitary gland and the midbrain by way of the circulation on the anterior lobe veins to the cavernous sinus, and thence by way of the general circulation. In opposition to this general path there exists a second local circulation which Roussy and Mosinger (1933) called *hémocrinie locale*. The anatomical investigations of Popa and Fielding (1930), suggested by Cushing's studies, furnished the basis for accepting a local circulation, a direct vascular link between the pituitary gland and the midbrain, called the "portal" circulation.

Apart from the investigations derived from anatomy, the significance of the nervous system is shown by certain data based on physiological and pathological researches. Of a number of various attempts which have been made, only one need be mentioned. The higher iodine concentration in the pituitary colloid (1200 to 1300 micromg per 100 cc., according to Noether, 1932) and in the whole pituitary gland (80 micromg per 100 cc., according to Sturm, 1928) and also in the midbrain (27 micromg per 100 cc.) than in the remaining regions of the brain (6 to 9 micromg per 100 cc., according to Sturm and Schneeberg, 1933) further the drop of the iodine concentration in the midbrain after thyroidectomy and hypophysectomy (Schuttenhelm and Eisler, 1933), and finally the rise of iodine concentration in the midbrain and medulla oblongata in animals injected with thyrotropic hormone (Pighini, 1935) and in patients dead from thyrotoxicosis (Sturm and Schneeberg, 1933) all seem to afford a basis for an iodine regulating center of the midbrain and its etiologic role in thyrotoxicosis. It is probably iodine or thyroid hormone passes from the pituitary colloid from the pituitary gland to the tuber cinereum, which in turn, on being stimulated, may exert an effect through the sympathetic and parasympathetic fibers. In connection with this, it should be mentioned that according to Dobrzaniecki and Aron (1930) the thyrotropic hormone cannot produce a picture of thyroid hyperfunction when the organism is deprived of parasympathetic fibers. This suggestion received some

support from experiments carried out by Fenz and Uiberrak (1937) which showed the inhibitory effect of midbrain narcosis, produced by the administration of barbiturates, on the thyroid gland in human thyrotoxicosis. These authors found a distinct and often prolonged fall of the increased blood iodine level normally observed in patients suffering from thyrotoxicosis.

Some other experiments, however tend to undermine the role of the nervous system. In contrast with Dobrzaniecki and Aron's experiments, Marine and Rosen (1934) have demonstrated on the one hand that thyrotropic hormone stimulates the autothyroid transplants as well. On the other hand the results of our recent investigations (Elmer Giedosz, Schepps and Weber unpublished data) do not fall into line with those of Fenz and Uiberrak. We injected the thyrotropic hormone into guinea pigs intraperitoneally for a six-to-ten day period and treated them simultaneously with Prominal or Luminal but we failed to see any inhibitory effects of the barbiturates on the hyperfunctioning thyroid gland. Nevertheless, we agree with Means (1937) that such observations limit rather than exclude a secretory function on the part of the nervous system.

The Role of the Liver

Having described the role of the separate intrinsic and extrinsic factors, I shall now enter into the real pathogenetic mechanism of thyrotoxicosis. Vogt-Moller (1931) in his work on the pathogenesis of thyrotoxicosis stated that the problem raised the question, Is there decrease in the elimination of the thyroid hormone, or in its destruction? This author was rather of the opinion that the alterations in the elimination of the thyroid hormone from the body are the more important in the mechanism of the pathogenesis of thyrotoxicosis. He suggested that the thyroid hormone secreted in excess by the thyroid gland results in damage to the kidneys, which in turn impedes the excretion of the hormone and thereby causes its accumulation in the body. We (Elmer, Giedosz and Schepps, unpublished data) could indeed find marked microscopic alterations in the kidneys in experimental permanent hyperthyroidism but before we can discuss the decrease in urinary thyroxine elimination as a real pathogenetic factor of thyrotoxicosis, it is necessary to show whether the thyroid hormone under physiologic conditions is eliminated in urine. Our investigations afford no basis for belief in elimination of thyroid hormone in this way. Hence, depressed elimination of the thyroid hormone in urine should be discounted as a pathogenetic factor of thyrotoxicosis.

However, the second of the possible pathoge-

netic factors, namely reduced power of destroying the thyroid hormone, seems to play a more important part. Hunt (1907) suggested, as a result of his experiments based on the acetonitrile test, that in thyrotoxicosis there is not only augmented secretion but also diminished destruction of the thyroid hormone in the body. Blum and Grutzner (1920) showed that the liver is the organ which possesses the power of destroying the thyroid hormone. Our investigations (Elmer and Luczynski, 1933) seem to point to the conclusion that this power is to some extent limited, even in healthy men, for after excessive administration of the thyroid hormone only a part of it undergoes decomposition. Thus we can easily imagine that in thyrotoxicosis, the increased content of the thyroid hormone in the blood may be due not only to its excessive secretion, but probably also to a slowing up of its decomposition due to diminished activity of the liver in this respect. This supposition receives strong support from a series of clinical and experimental investigations, which give grounds for accepting the view that in thyrotoxicosis the liver undergoes injury under the influence of long-continued secretion of the thyroid hormone in excess. Very remarkable histologic alterations in the liver have been found in human thyrotoxicosis by numerous authors, in particular Beaver and Pemberton (1933). Hepatic injuries are manifested by enlargement or atrophy of the liver, subicterus, a positive galactose test, reduced glycogen content in the liver, hyperketonemia, increased amounts of urobilinogen in the feces and the urine and so forth. In agreement with these observations, the results of our investigations afford the basis for accepting the pathogenetic role of the liver in thyrotoxicosis. In experimental maintained hyperthyroidism we found severe histologic alterations of the liver, which occurred without exception in all animals treated with increasingly large doses of the thyrotropic hormone. The decrease in cholesterol ester in the blood and in glycogen in the liver, observed always in the advanced course of the experimental hyperthyroidism, falls into line with the histopathologic alterations of the liver.

SUMMARY

In the etiology and pathogenesis of thyrotoxicosis both intrinsic and extrinsic factors should be considered.

An intrinsic abnormality of the thyroid gland would be a condition in which the gland either primarily has lost its ability to retain the elaborated hormone or is producing an altered hormone. The conception that in the normal gland there is an equilibrium between thyroxine and diiodotyrosine, which in primary hyperthyroidism is disturbed by thyroxine's becoming predominant, lacks any substantial clinical or experimental support.

With regard to the second possibility of the secretion of an altered hormone, the hypothesis of elaborating less-iodized hormone is no longer tenable, and the conception of dysthyroidism, based on the secretion of an otherwise altered hormone, will have to wait upon further experimental evidence.

An extrinsic abnormality of the thyroid would be a condition in which the gland is overproducing the hormone owing to the alterations in other organs. Of many possible extrinsic factors only some play an important part. Evidence for the role of a hyperfunctioning anterior lobe of the pituitary gland in human thyrotoxicosis has been furnished by the author and his associates, who succeeded in inducing an experimental maintained hyperthyroidism in dogs and guinea pigs by injecting the thyrotropic hormone in increasingly large doses.

The significance of the nervous system, in particular of the midbrain, in thyrotoxicosis is also shown by certain data, but its part is limited. The gonads, particularly the ovaries, seem to exert their effect only through the anterior lobe of the pituitary gland. The hypothesis of the primary insufficiency of the adrenal cortex must be rejected.

There is not sufficient justification for accepting the primary role of vitamin deficiency. The hyper-*vitaminoses* may result either from secondary increase of the consumption of vitamins or from their reduced absorption due to disturbances in the alimentary canal. The liver damage constantly found in experimental permanent hyperthyroidism and frequently in human thyrotoxicosis plays a very important part in the pathogenesis of thyrotoxicosis. The discrepancy between the excessive production of the thyroid hormone by the thyroid gland and the slowing up of the destruction of the hormone by the liver results in an accumulation of the thyroid hormone in the body, with symptoms of thyrotoxicosis.

PINWORMS AND APPENDICITIS*

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THIS paper presents our conception of the relation of *Enterobius vermicularis* infection|| of the vermiform appendix to appendicitis in children. That pinworms occur in the appendix has been known for a long time, as Fabricius¹ in 1634 and Sontorini² in 1724 described the condition. Only in the last forty years, however, has any active interest been shown in this subject, further more, a perusal of the literature leaves one in doubt as to the status of pinworms in relation to appendicitis. The material in this report has been obtained from the 71 cases in which *E. vermicularis* infection was discovered in appendices removed at operation at the Children's Hospital, Boston, from 1929 to 1939.

THE PARASITE

E. vermicularis is a small, white, round worm³. The male measures 2 to 5 mm in length and the female 9 to 12 mm. The worms when young live in the small intestine, but in the adult state they live in the colon. Copulation takes place in the intestine, the gravid female migrating outside the anus or being expelled at defecation. The eggs are deposited outside the host and the female dies. The eggs enter no intermediate host and develop after re-entering a human host. Autoinfection is quite common, there is, however, some evidence²⁻⁴ that reinfection may occur within the gastrointestinal tract. The exact length of the life cycle of the parasite in man is not known. 'enso' states that it is about twenty days. The diagnosis of pinworm infection is made by finding the worms or ova in the stools, or by finding the ova in anal scrapings or under the finger nails. An intradermal test for pinworm infection has been devised,⁶ but its present value is doubtful. Microscopical examination of anal scrapings is the most reliable diagnostic aid.

INCIDENCE

Pinworm infection is very common in children. A recent survey at the Children's Hospital revealed that approximately 18 per cent of the patients harbored pinworms.⁶ This rate corresponds roughly to that given in other reports.⁷⁻⁹

In the ten year period 1929-1939, 1343 appendices were removed at this hospital. Pinworms were found in 71 (5.3 per cent). Beck⁸ reports an incidence of 2.0 per cent in 1718 appendices, Gordon¹⁰ 1.2 per cent in 26,051, Goodale¹¹ 6.1 per cent in 1369, Warwick¹² 1.9 per cent in 2344.

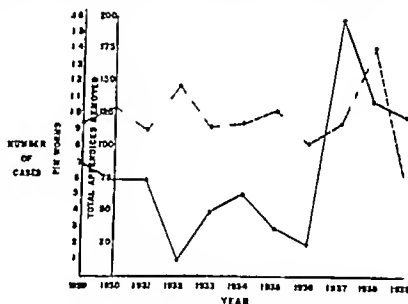


FIGURE 1. — Pinworms. Total appendices removed

and Andr ¹³ 6.7 per cent in 2651. It is of interest that in our series the condition was most frequently present in December, January, March and September, and that acute appendicitis was also most frequently seen in those months, with the exception of January.¹⁴

There has been a marked increase in the number of appendices found to be infected with pinworms during the last three years, although the total number removed each year has been relatively constant (Fig 1). We believe that the increase is due to a more thorough search for the parasite in the appendiceal contents. This examination consists of a microscopical search as well as a gross inspection. Only by this method can the male

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||The term "infection" is applicable wherever the parasite larvae and establishes itself within the body of the host including in this case the gastrointestinal tract.

worm be recognized, whereas the female can be seen with the naked eye. The incidence of appendices containing pinworms would be higher if such a procedure were followed routinely in other hospitals as this figure has more than doubled at this hospital since microscopical examination was included.

AGE AND SEX

The ages of our patients varied from eighteen months to twelve years. There was a noticeable increase in the number of cases at the age of five and again at the age of eight (Fig 2). These in-

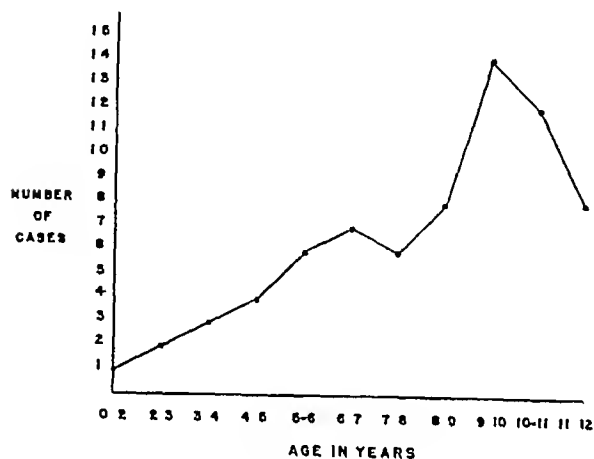


FIGURE 2

creases correspond to the ages when children have more opportunity to be infected with the parasites. Girls are more commonly infected than boys.^{1, 11} In this series there were 45 girls and 26 boys.

CLINICAL CLASSIFICATION

The cases fall naturally into two groups. In Group I are the patients who had acute appendicitis, while Group II includes the cases in which histologic evidence of the condition was lacking. *E. vermicularis* was present in varying numbers in all the appendices of both groups.

Group I

In a total of 848 cases of acute appendicitis, there were 26 appendices containing pinworms. The diagnosis of acute appendicitis was confirmed in all cases by operation or pathological examination, and is the subject of a report by Hudson and Chamberlain.¹⁴

Twenty-five* patients entered the hospital because of abdominal pain of several hours' to several days' duration (Table 1). The pain was usually referred to the umbilicus and was cramplike. Nausea followed by vomiting was present in 18

*The twenty-sixth patient had had acute appendicitis with peritonitis three months before being admitted for interval appendectomy. At the time were performed.

cases (69 per cent). In no case was there a history of pinworm infection. Only 7 patients (27 per cent) had had previous attacks of abdominal pain. This corresponds closely to the incidence of previous attacks of pain in children with acute appendicitis without pinworm infection.¹⁴ Those attacks had occurred from one month to one year previously, with most of them two to four months before.

TABLE 1 Patients with Acute Appendicitis and *E. vermicularis* Infection

CLINICAL DATA	NO OF CASES
Previous attacks of abdominal pain	7
No previous attacks of abdominal pain	19
Nausea and vomiting	18
Nausea but no vomiting	3
No nausea or vomiting	3
Tenderness and spasm in right lower quadrant	22
Tenderness but no spasm in right lower quadrant	3
No abdominal tenderness or spasm	1
Temperature (rectal)	
102-101°F	6
101-100°F	7
100-99°F	13
Leukocyte count	
25,000-20,000	7
20,000-15,000	6
15,000-10,000	10
10,000-5,000	5
Not recorded	3

Physical examination revealed tenderness and spasm in the right lower quadrant in 22 cases (95 per cent), in 3 of the remaining 4 cases there was tenderness but no spasm. The leukocyte count was above 10,000 in 18 cases. Search for eosinophilia was not made in any case. In most cases the rectal temperature was between 99 and 101°F.

A diagnosis of acute appendicitis was made and followed by immediate operation in 24 cases. One patient, mentioned above, had been operated on at another hospital. Another did not show sufficient signs on entry to justify the diagnosis, operation was performed two days later and a subsiding appendicitis was found. In 4 cases the appendix had ruptured and peritonitis was present. There were no deaths in this group.

The pathological examination of the appendices revealed no evidence that *E. vermicularis* was the initiating factor.¹⁵ From the clinical aspect the cases did not differ from the usual picture of appendicitis seen in children.¹⁴

Group II

Of 495 appendices described by the pathologist as presenting no inflammatory reaction, 45 harbored pinworms. Forty-four patients* complained of abdominal pain (Table 2). There was no history of previous pinworm infection in any case. A history of attacks of abdominal pain prior to entry was

*The forty-fifth patient was operated on because of an ovarian tumor and the appendix was removed incidentally.

obtained from 30 patients (67 per cent). In 848 cases reported by Hudson and Chamberlain,¹⁴ only 30.5 per cent of the children with acute appendicitis had had preceding attacks of abdominal pain. In our series the attacks of pain dated as far back as four years in 1 case and two years in 9. In the remainder pain had been first noticed from one to twelve months before. Most of these patients were old enough to describe their pain, and stated that it was cramplike and occurred in the umbilical region. The length of the attacks varied considerably with each patient. It is

TABLE 2. Patients with *E. vermicularis* Infection of the Appendix but without Histological Evidence of Appendicitis

CLINICAL	N.O. OF CASES
Previous attacks of abdominal pain	30
No previous attacks of abdominal pain	15
Nausea and vomiting	25
Nausea but no vomiting	4
No nausea or vomiting	12
Tenderness and spasm in right lower quadrant	9
Tenderness but no spasm in right lower quadrant	28
No abdominal tenderness or spasm	1
Temperature (rectal)	
102-101 F	7
101-100 F	9
100-99 F	29
Leukocyte counts	
25,000-30,000	5
20,000-25,000	2
15,000-20,000	22
10,000-15,000	14
Below 10,000	2
None recorded	

important to note that 32 patients (71 per cent) entered the hospital in acute attacks of pain as emergency cases, and that only 13 (29 per cent) entered for investigation of chronic abdominal pain.

Nausea and vomiting were present in 25 cases (56 per cent) and nausea alone in 8 (18 per cent).

The rectal temperature was below 100°F in most cases although 7 patients had temperatures of over 101°F. Physical examination revealed tenderness alone in the right lower quadrant in 28 cases (62 per cent), tenderness and spasm in 9 (20 per cent) and no abdominal tenderness or spasm in 8 (18 per cent). The leukocyte count was usually between 10,000 and 20,000. Search for eosinophilia was made in 16 cases; it was noted in only 1, in which the eosinophils were listed as 15 per cent.

A diagnosis of acute appendicitis was made and an immediate operation performed in 22* (69 per cent) of the 32 emergency cases. Elective appendectomy was performed in the others.

Pathological examination of the appendices of this group revealed no anatomic or inflammatory

change attributable to *E. vermicularis*¹⁵ except in 3 cases where portions of pinworms were found in the submucosa. This finding has been reported frequently.¹⁶

DISCUSSION

Cases of acute inflammation and pinworm infection of the appendix cannot be regarded as different in any particular from those of acute appendicitis without pinworm infection. In our series there was no clinical or pathological evidence justifying any other belief. However, various authors^{7, 12, 16-18} believe that the parasites provide a mode of entry for pathogenic bacteria by burrowing into the wall of the appendix and thus initiate true acute appendicitis. It is known that such penetration does occur. This was true in 3 cases in the present series, but no inflammatory reaction was present.¹⁸ Gordon,¹⁰ after a careful pathological study of appendices infected with pinworms, concluded that the worms had migrated after the appendix had been removed, and found no inflammatory reaction in any case. The evidence, using histological studies as a standard, at present is equivocal as to whether or not pinworms initiate acute appendicitis.

The main problem however, is presented by those patients who show the signs and symptoms of appendicitis and have pinworm infection of the appendix, yet give no histological evidence of appendicitis. Since in the vast majority of cases histological evidence of tissue reaction due to the parasite is absent it is difficult to state how the worms cause symptoms. It has been suggested that the symptoms are due to penetration of the wall of the appendix by the worms,²⁰ or that the parasite causes a local toxic reaction in the appendix.²¹ On several occasions we have seen the worms sticking into the submucosa when the appendix was opened immediately after removal. Despite the lack of knowledge concerning the mode of action of pinworms in the appendix, most authors^{7, 9, 12, 16, 18-22} think that the parasites must be responsible for the syndrome. The fact that patients who have complained of recurrent bouts of abdominal pain and who have pinworms in the appendix are relieved when the appendix is removed is strong evidence for this opinion. In our series a careful check up of 29 of the 30 patients who had had recurrent abdominal pain and pinworms in the appendix revealed that in no case was there recurrent pain after appendectomy.

The clinical diagnosis of pinworm infection of the appendix cannot be made with certainty. It may be suggested by the picture given by Wood—

"The histories of my cases were long and inter

*One patient had primary streptococcal peritonitis. The appendix was removed when the peritoneal cavity was drained, and the patient died. This is the only death in the group. Disease of the appendix was not the cause of the peritonitis.

mittent, vomiting was often absent, the temperature was usually normal or only slightly raised and the leukocytosis was slight." To this may be added a history of pinworm infection. Eosinophilia is of diagnostic value, but in our experience it was present in only 1 of the 16 cases in which it was looked for. A large number of patients, however, present a history and physical examination exactly like those of acute appendicitis, and there is no course except to treat them as cases of appendicitis. As a general rule it is not safe to attempt to treat with vermifuges patients who have appendiceal symptoms which may be caused by pinworms. In the first place, the diagnosis may be incorrect and the patient may have acute appendicitis, in the second place, the vermifuge may not act on the worms in the appendix.

SUMMARY AND CONCLUSIONS

Seventy-one of 1343 appendices removed at the Children's Hospital, Boston, from 1929 to 1939 were infected with pinworms.

Microscopical as well as gross inspection of the appendiceal contents is advocated in order to find the parasites.

Twenty-six patients had acute appendicitis and pinworm infection. The cases differed in no way from the usual picture of acute appendicitis in children.

Forty-five patients had no inflammatory change in the appendix but had pinworm infection. All had abdominal pain and all were relieved by appendectomy.

Twenty-nine of the 30 patients who had chronic abdominal pain were relieved by appendectomy.

Twenty-two patients who had no histological evidence of appendicitis but had pinworm infection

of the appendix presented a syndrome exactly like that of acute appendicitis.

Pinworm infection of the appendix cannot be differentiated with certainty from acute appendicitis. It may be suggested by a history of pinworm infection and recurrent abdominal pain.

The mechanism of the mode of action of pinworms in the appendix is unknown.

The safest treatment of appendiceal symptoms due to pinworms is appendectomy.

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ROCKY MOUNTAIN SPOTTED FEVER

A CASE REPORT

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ROCKY Mountain spotted fever is an acute disease rarely seen in this immediate area, although for several years it has occurred sporadically in the eastern states. It is fairly common in the District of Columbia and Maryland where the case here reported is presumed to have originated. The disease was originally described by Maxey¹ in 1899 in an article read before the Oregon State Medical Society, when he referred to it as spotted fever. In 1902 Wilson and Chowning² suggested the theory of transmission by ticks and referred to the condition as spotted fever of the Rocky Mountains. In 1903 Anderson³ referred to the condition as tick or spotted fever of the Rocky Mountains. Although especially common in the Rocky Mountain region and particularly in the Bitter Root Valley of Montana, it has of late been found in various communities throughout the United States and Canada. The work of Pinkerton and Hass⁴ has established the relation between boutonneuse fever and the Eastern variety of spotted fever of our country.

This disease belongs to the typhus-like group of conditions due to rickettsial infections transmitted by ticks, mites, lice and fleas. The inoculation of the virus through the bite of an infected wood tick produces exanthematous tick fever, commonly called Rocky Mountain spotted fever. Man does not contribute to the perpetuation of the virus in nature as in the case of malaria or yellow fever. Instead the virus is propagated by infection of an animal host by the tick in the process of feeding the animal then infecting other ticks, or through hereditary transmission by the female tick to her eggs. While a large percentage of cases undoubtedly occur as a result of a tick bite, infection may come about by contact with material from crushed, infected ticks. The importance of this is illustrated by the case reported here with

The animal hosts vary in different sections of the country. In New England they include chipmunks, woodchucks, rabbits and field mice. While dogs frequently carry ticks, it is not yet considered certain that they serve as a reservoir of the disease.

In 1906 Ricketts⁵ began a study of Rocky Mountain spotted fever, and continued it until his death in 1910 from the rickettsial disease, typhus fever. He was able to infect *Dermacentor* ticks by feeding them on guinea pigs inoculated from a patient suffering with Rocky Mountain spotted fever. In 1931 *Dermacentor variabilis* was found to be the carrier of tick fever in the eastern United States.⁶ This tick passes through larval, nymph and adult stages. In its more immature forms it feeds on mice, rabbits and chipmunks, thereupon dropping off the host for the purpose of molting. The adults frequently attach themselves to dogs. The tick usually climbs up on grass or shrubbery and fastens itself to a passing host, animal or human.

In 1916 Wolbach⁷ made a search among infected ticks for the causative agent of Rocky Mountain spotted fever, and found a gram negative *Rickettsia* in all tissues of infected ticks and in the vascular lesions of infected animals. This was subsequently confirmed by other investigators and the agent was called *Dermacentroxenus rickettsii*.

Before 1930 it was thought that this disease did not exist in the eastern United States, but in 1931 a number of cases were reported from this section.⁸ Ticks have been found to be very prevalent on Cape Cod, Massachusetts, and several cases have occurred there in the last two years.⁹ Summer residents often find ticks on themselves and on their dogs, and remove them. Occasionally the insects are found on bed linen left on the ground or hung so as to touch the grass or shrubs. The importance of protecting the hands when removing ticks, especially when the insect has been crushed, cannot be overestimated. Likewise, protection of the body, particularly the legs, when traveling through the grass or brush, and the examination of linen left out of doors should be made routine in sections where ticks are prevalent. The tick season in the eastern United States extends from the first warm days of spring to midsummer.

Recovery from Rocky Mountain spotted fever is believed to produce prolonged immunity although cases of re-infection have been reported. The mortality varies but is frequently high. For example, of 4 cases reported in New York in 1936, 2 were fatal, and of 4 cases reported in the District of Columbia in the same year, 2 were fatal.

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CASE REPORT

A 35 year-old housewife was seen at home by one of us (N A W) on June 20, 1938, with complaints of malaise, severe headache, generalized muscular aching and fever. The temperature was 103°F. Physical examination was negative except for tenderness over the region of the left kidney. Urinary examination showed a moderate number of pus cells, so that a probable diagnosis of pyelitis was made. The following day an irregular macular eruption appeared on the arms and scattered areas of the body. At that time it was learned that the patient had returned home on June 17 from a visit to Maryland near the District of Columbia border. While there, some time between June 5 and 12, she removed five ticks from a dog, some being crushed in the process. It is interesting to note that a short time previously the dog had been transported from Texas. The patient had no knowledge of any tick bite. The day after her return the patient began to complain of exhaustion and headache.

The rash became fairly widespread and involved the hands and feet. The temperature ran between 103 and 104.5°F with no remission, and there was continuous severe headache. The patient gradually became lethargic, falling asleep even while being bathed. However, she could be easily roused. The skin became hypersensitive for a short time about a week after the onset of the rash, and a marked conjunctivitis with photophobia developed. The rash assumed a purplish red appearance, and was particularly evident in areas of pressure such as those over the scapula regions, over the buttocks and on the dependent surfaces of the arms.



FIGURE 1 *Spotted Fever Rash on Arms*

On June 22 the patient was examined by Dr. Fred Bailey, of the Boston Health Department, and Dr. Henry Pinkerton, of the Harvard Medical School. Inoculation of guinea pigs with specimens of blood taken at that time yielded results which were consistent with a diagnosis of spotted fever. Subsequent cross-immunity tests with a virulent spotted fever culture at the Department of Bacteriology, Harvard Medical School, demonstrated the existence of spotted fever antibodies in the patient's serum.

The patient was admitted to the Carney Hospital on June 29, 1938, in essentially the lethargic state described above. On July 4 she began to show remissions in the fever, and on July 9 she was running a normal temperature, which continued until her discharge on July 19. The residual of the rash persisted for several months, and as late as October was easily visible on the legs when standing and on the arms on the application of a tourniquet.

During the height of the illness the pulse was between 120 and 130, although it had been practically normal in

the early stages of the disease. The respirations were close to 40 for several days, although nothing to account for the increase was ever demonstrable in the lung fields. The white-blood-cell count was never high, at the onset it was only 10,000, and on admission it was 12,200, the highest count obtained. The red-cell count ran between 3,440,000 and 3,900,000, with a hemoglobin of 68 per cent. The polymorphonuclears averaged 88 per cent.

Treatment with an adequate blood concentration of sulfanilamide resulted in no improvement. The rest of the treatment was symptomatic and supportive.

This case is reported because of the rare occurrence of Rocky Mountain spotted fever in Massachusetts, and because its severe nature warrants



FIGURE 2 *Spotted Fever Rash on Legs*

calling the attention of the medical profession to the possibilities of its prevention. Clinically the disease is indistinguishable from endemic typhus fever, but according to Pinkerton¹ the appearance of a rash on the soles and palms suggests it rather than typhus fever, in which such distribution is usually absent. The case also demonstrates the probability of infection without the actual bite of a tick. It suggests the advisability of prohibiting the interstate transportation of dogs during the tick season if it can be shown that such animals are reservoirs of rickettsial infection.

SUMMARY

Rocky Mountain spotted fever is becoming commoner in the eastern states as a result either of local infection or of the entry of persons who have acquired the infection elsewhere. The case here reported showed the typical symptoms and signs of severe headache, conjunctivitis, high persistent temperature, elevated respirations with no demonstrable pulmonary cause, lethargy and characteristic embolic rash, with persistent evidence of the last for a long time after the subsidence of the infection. The progress of the case was not influenced by the use of sulfanilamide.

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REPORT ON MEDICAL PROGRESS

VASCULAR DISEASES WITH PARTICULAR REFERENCE TO ARTERIAL HYPERTENSION*

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INVESTIGATORS in the field of physiology and the diseases of the peripheral vessels have been active in recent years. Progress in this field has been extensive.

METHODS

Stead and Kunkel¹ have devised a plethysmographic method for the quantitative measurement of the blood flow in the foot. The inherent error of this method is about 3 per cent. When the measurements are conducted at a temperature of 43°C., maximal dilatation of the vessels develops and therefore the maximal blood flow is measured. In 34 normal subjects the average blood flow was 171 cc. per minute per 100 cc. of tissue. The lowest value was 111 cc., and the highest 259 cc. The values were somewhat lower for men than for women. Comparative measurements indicated a considerably smaller reserve in the blood flow in the foot than in the hand. In the presence of arteriosclerosis and thrombo-angitis obliterans the blood flow may be reduced to 50 per cent of normal before local symptoms or signs develop. When the blood flow reaches as low a level as about 5 cc. per minute per 100 cc. of tissue, or one third of normal trophic disturbances are apt to appear. This method offers opportunity for a more precise study of a number of pertinent vascular problems.

Sodeman and Burch² have described a simple method which measures the distensibility of the skin with the aid of a small caliper of known calibration. In the presence of edema the distensibility decreases, and this is a factor in limiting the formation of edema. Changes in the distensibility have been found in a number of cutaneous dis-

eases such as senile atrophy, allergic eczema and scleroderma.

Wright, Schneider and Ungerleider,⁴ on the basis of questionnaires sent to medical schools, life insurance companies and individual physicians, have pointed out the great variations existing in the technique of measuring arterial pressure. To remedy this they suggested an investigation of this problem by a national committee. This has actually been done recently.

Committees appointed by the American Heart Association and by the Cardiac Society of Great Britain and Ireland recommend the following procedure as the standard method for taking blood pressure readings in man.⁴

Blood Pressure Equipment. The blood-pressure equipment should be in good condition and calibrated at yearly intervals. Under these circumstances either mercurial or aneroid types of apparatus are capable of correct readings. The mercury manometer should be checked at intervals so as to be sure that the level of the mercury at rest is at the zero mark and that the air vent at the top of the glass tubing is not clogged. When readings are taken the apparatus must be on a flat surface at the level of the observer's eyes.

The Patient. The patient should be seated with the arms slightly flexed and the whole forearm supported at heart level. If readings are taken in any other position notation should be made. The patient should be allowed time (ten to fifteen minutes) to recover from any recent exercise or excitement. The time of day should be recorded.

Position and Method of Application of the Cuff. A standard-sized cuff 12 to 13 cm. in width should be used. The completely deflated cuff should be applied snugly and evenly around the arm with the lower edge about 3 cm. above the antecubital space and with the rubber bag applied over the inner aspect of the arm. Inflation should not cause bulging at the edges of the cuff. Special cuffs of suitable size should be used for the measurement of blood pressure in the leg or in children.

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Checking Palpatory and Auscultatory Levels The pressure in the cuff should be quickly increased in steps of 10 mm of mercury until the radial pulse disappears, and then allowed to fall rapidly. If the radial pulse returns at a higher level than that at which the first sound is heard, the palpatory reading should be accepted as the systolic pressure.

Application of Stethoscope The stethoscope should be placed over the previously palpated brachial artery in the antecubital space, not in contact with the cuff. The lip of the stethoscope should make contact with the skin but with a minimum of pressure.

Determination of the Systolic Pressure The cuff should be rapidly inflated to a pressure about 30 mm above the systolic pressure and then deflated at a rate of 2 to 3 mm of mercury per second. The level of the first sound should be considered the systolic pressure unless the palpatory level is higher. All unnecessary venous congestion should be avoided. It is well to take the blood pressure in both arms on the first examination. With premature beats the higher systolic pressure of the beats that terminate compensatory pauses should be ignored. With auricular fibrillation the average of a series of readings may be used.

Determination of the Diastolic Pressure and the Pulse Pressure With continued deflation of the cuff, the point at which the sounds suddenly become dull should be known as the diastolic pressure. If this point differs from that at which the sounds disappear, it is recommended that both points be recorded, for example, 140 systolic, 80-70 diastolic. If these two levels are identical the blood pressure should be recorded, for example, 140 systolic, 70-70 diastolic.

Montgomery and Starr⁶ have described the use of four simple apparatus in the treatment of vascular diseases. These are a foot cradle provided with a thermoregulator for the maintenance of heat over the lower extremities, a simple instrument for the administration of iontophoresis, a specially constructed bed for the comfort of patients with vascular diseases of the lower extremities and a small suction apparatus devised for the fingers.

ARTERIAL HYPERTENSION

So far as the etiology of hypertension is concerned, more evidence has been brought to light on the importance of renal ischemia in several types of hypertension.⁷ Rytand⁸ has demonstrated, with the aid of ingenious animal experiments, that renal ischemia is responsible for the hypertension of coarctation of the aorta. Weiss and Parker⁹ in a systematic study of the natural history of pyelonephritis have investigated the relation of the disease to arterial hypertension. They claim that the inflammatory reactions of the tissues are responsible for the development of hyperplastic arteriolosclerosis not only in the active but also in the healed cases of pyelonephritis. A relation was found between renal vascular changes and arterial hypertension. The hypertension associated with chronic pyelonephritis can be malignant in type. It has been estimated that pyelo-

nephritis is responsible for 15 to 20 per cent of the total number of cases of malignant hypertension of varied origin. Weiss and Parker call attention to the fact that pyelonephritis, particularly in its chronic stage, should be considered as one type of Bright's disease.

Wiggers¹⁰ has reviewed the present knowledge on the dynamics of the circulation. He points out the similarity between the hemodynamics and the vascular states of certain types of experimental and human hypertension. He believes that renal hypertension in man is caused by humoral and not by nervous factors. The most important resistance in hypertension is located in the arterioles and in the prearterioles, but Wiggers enumerates evidence indicating that changes are present also in the larger arteries. Decreased elasticity of the aorta and other arteries is responsible in part for the high pulse pressure and marked elevation of the systolic pressure.

Tigerstedt and Bergman¹¹ demonstrated in 1898 the existence of a vasopressor substance in the kidney, called renin. Recent interest¹²⁻¹³ in the renal causation of hypertension has redirected attention to the specific role of this substance. It is too early to claim, however, that renin is the humoral agent responsible for the renal type of arterial hypertension. Hessel¹⁴ reports a detailed study on the action of renin. He observed that following the daily injection of renin for a period of five weeks or over, elevation of the arterial pressure persisted as long as seven months. It is particularly significant that he was able to demonstrate the presence of this substance in the venous blood of the kidney. Prinzmetal, Friedman and Abramson¹⁵ found more pressor effect after the injection of saline extracts of ischemic kidneys than after injection of a similarly prepared extract of the normal contralateral kidney. A number of additional reports of less importance have been published on the presence and action of renin in different species of animals. It is of interest that transfusion of the blood of patients with malignant hypertension failed to produce elevation of the arterial pressure in normal subjects.¹⁶

In the evaluation of therapeutic measures in hypertension, lack of information on the natural history of the condition is a handicap. It is for this reason that the contribution of Hines¹⁷ is significant. He reports on the level of the arterial pressure of 1185 persons from ten to twenty years after the initial reading. The majority of patients with elevated pressure at the first measurement had developed increasing pressure, while only a relatively small percentage of those with normal readings at the start showed hypertension.

So far as the vascular lesions are concerned, it

has been demonstrated again that various types of arteriolar and arterial lesions are apt to be present in a number of organs in the presence of hypertension¹⁸⁻⁹

In the chemotherapy of hypertension no significant advances have been made. The therapeutic value of various types of sympathetic surgery is still unsettled, notwithstanding optimistic reports. Craig²¹ claims that 70 per cent of the cases have been benefited by subdiaphragmatic section of the splanchnic nerve. This is in agreement with the results obtained by Freyberg and Peet,²² who claim that in approximately 60 per cent of their cases the blood pressure was lowered at least for several months. Moore² sectioned the splanchnic nerve in 22 patients. A lowering in the blood pressure was maintained for over a year in 45 per cent of the cases. Before a final answer can be given on the specificity of surgical operation certain types of control studies are essential. From such a point of view the observations of Volini and Flaxman²⁴ are of interest. These investigators, impressed by their belief that the majority of proposed therapeutic measures rapidly pass into obscurity, undertook a comparative evaluation of the results of nonspecific surgical measures (hysterectomy, cholecystectomy and prostatectomy) and of specific neurosurgical operations such as extensive sympathectomy, splanchnic nerve resection and celiac ganglionectomy. They followed the effects of operations on 52 hypertensive patients. Twenty-seven of these were suitable for analysis. Reduction of blood pressure following the nonspecific operations was common. Symptomatic improvement was a usual feature in the group. Regardless of the type of operation, all patients were relieved of symptoms such as headache, nervousness, dizziness, fatigue, insomnia and palpitation for four months to nine years. These authors assert that the results obtained by specific operations can be duplicated by non-specific surgical measures.

Partial constriction of one renal artery in animals results in marked and sustained hypertension. If the kidney, corresponding to the constricted artery, is excised such hypertension is abolished. The physiologic principle involved in these experiments has a distinct therapeutic applicability. Cases of unilateral renal ischemia associated with arteriosclerosis or congenital hypoplasia of the renal artery, and those with unilateral inflammatory kidney disease, are quite frequent. Reports²⁵⁻²⁷ on successful abolition of arterial hypertension following surgical removal of such unilaterally diseased kidneys are appearing in increasing numbers. This surgical procedure is a rational one, but the follow up period of the cases

operated is too short to warrant a final expression of opinion.

In animals with constricted renal arteries efforts have recently been made to improve the renal circulation and reduce the hypertension through experimentally induced collateral circulation. This procedure has not been applied to the treatment of human hypertension although a clinical report²⁸ on the beneficial effects of omentonephropexy has appeared.

ARTERIOSCLEROSIS

The etiology of arteriosclerosis is still an unsettled problem. In a systematic investigation Winternitz, Thomas and LeCompte²⁹ have emphasized the concept that hemorrhage within the vascular wall represents a significant source for the development of lipid deposits and subsequently atheromatous plaques. They discuss in detail considerable indirect evidence in favor of this assumption. They present a method for the demonstration of the vascular network in the intima of vessels of animals and of man. Leary³⁰ has also reported on the vascularization of atherosclerotic lesions. The normal intima is not vascularized and vascularization develops only as a part of the repair process. In his experience internal hemorrhages play no etiologic role, because they represent late phenomena. Cholesterol is carried to the site of vascular deposition in macrophages, the presence of the latter not being due to local vascular hemorrhages.

In a group of 100 diabetic patients Kramer³¹ found the incidence of arteriosclerosis to be 38 per cent. Roentgen-ray studies of the extremities revealed calcified vessels in 63 per cent of the cases of arteriosclerosis. It is of interest that only 21 per cent of the arteriosclerotic group showed elevated lipid content of the blood. The simple histamine test was found to be useful in the estimation of the degree of collateral circulation. Stroud and Shumway³² found that in a group of 57 patients with coronary occlusion 7 had suffered from intermittent claudication while in a group of 106 patients without heart disease only 1 was so affected. Patients with hypertension are more apt to complain of cramps at night than are normal persons.

RAYNAUD'S DISEASE

In the light of recent investigations this condition is considered a special type of sclerosis of the small arteries of the digits. Lewis³³ has studied the disease diligently and has recently reported again on his experiences. A comparative study of the arterial lesions of the fingers revealed that in patients with quite severe spasm the intimal thick-

ening, though pronounced, was no greater than that in subjects who suffered no symptoms. It is assumed that in such patients the muscular layer is overactive in response to certain types of stimuli. In cases with intermittent attacks associated with unhealed necrosis, thrombosis of the arteries was frequent. Lewis considers Raynaud's disease a manifestation of an occlusive structural disease, and not the result of an overactive vasomotor system. Preganglionic sympathectomy in 6 cases failed to abolish the local abnormality.³⁴ The initial temporary postoperative vasodilatation disappeared within as short a time as one week.

THROMBO-ANGITIS OBLITERANS

An extensive statistical analysis of 948 cases with thrombo-angitis obliterans has been presented by Horton.³⁵ It is of interest that twenty-eight nationalities were represented, and only 28 per cent of the patients were Jews. As high as 98 per cent were men. Ninety-three per cent consumed tobacco. The mean age of the men was 41.8 years and of the women 38.8 years. In a study of the causation of death in a group of 175 patients, 47 were shown to have died as a result of coronary heart disease, 12 of cerebral hemorrhage, 12 of gangrene or following amputation and 7 of fatal pulmonary embolism. A significant study on the cerebral manifestations of thrombo-angitis obliterans is presented by Hausner and Allen.³⁶ In a group of 500 patients with peripheral vascular involvement, 11 patients with clinical evidence of cerebral vascular involvement were observed. Usually the cerebral symptoms appeared after the manifestation of difficulties in the extremities, but in 3 patients cerebral symptoms preceded peripheral vascular insufficiency. The commonest manifestation of cerebral involvement was transient or permanent hemiplegia. Transient confusion, aphasia, disorientation and loss of memory were also present. Hemianopia was present in 2 patients.

The role of smoking in thrombo-angitis obliterans is still unsettled. Westcott and Wright³⁷ deny that patients with thrombo-angitis obliterans show a higher incidence of positive cutaneous reactions than do those in the control group. Harkavy,³⁸ on the other hand, claims that 70 per cent of the patients exhibit increased sensitivity. A study of serum calcium, serum protein, blood urea, serum lecithin, serum phosphorus, blood fatty acids and blood cholesterol failed to reveal significant changes in a study of 105 patients by Roth, Maclay and Allen.³⁹

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 25501

PRESENTATION OF CASE

First Admission A fifty-five-year-old lawyer was admitted to the hospital complaining of peridie epigastric distress.

About twenty years before admission the patient began to experience brief periods of epigastric distress, relieved by the ingestion of a soft bland diet. A detailed history of the attacks could not be obtained, but there was no vomiting, no nausea and no melena, and his bowels were normal. Twelve years before entry following a six-week sojourn in France where he ate freely, he had had an attack of diarrhea with black stools and slight gastric distress. By the time he received a medical examination his stools were free of blood, his symptoms responded promptly to treatment. Since that time he had had spells of nausea, vomiting and gastric distress lasting a few days to a few weeks. These were always preceded by periods of business strain; he characteristically reacted first emotionally then gastrointestinally. Each attack cleared with ample sedation and a bland diet, which was rapidly increased both in amount and in types of food. Six years before entry a duodenal ulcer was demonstrated roentgenologically, and an outside gastric analysis showed a free acid of 25 units, a total acid of 40 units and no blood. Four years before admission a two-hour diet with alkaline powders brought relief to attacks of upper abdominal gnawing pain which recurred every two hours. These attacks usually occurred in the spring and fall and were supposedly never precipitated by dietary carelessness. The symptoms increased progressively however until eight months before entry when he developed severe, persistent vomiting, with epigastric pain which proved intractable to treatment. He vomited everything including atropine, and progressed into an unquestioned temporary psychosis, as shown by excitement and disorientation as to time, place and people. From this he emerged fairly quickly and was placed on a bland diet. One month later he was eating practically everything and was well except for slight residual weakness. He had a similar attack a few days before admission. Physical examination revealed a well-developed

and nourished man. The heart, lungs and abdomen were normal. The blood pressure was 130 systolic, 80 diastolic.

The temperature, pulse and respirations were normal.

The examination of the urine showed a specific gravity ranging from 1.010 to 1.014 and the slightest possible trace of albumin. The sediment had 3 white blood cells, a rare red blood cell and numerous bacteria per high power field. The blood nonprotein nitrogen was 58 mg per 100 cc., and the blood chlorides 522 mg. Roentgenograms of the gall bladder by the Graham technic failed to show any evidence of stones. A gastrointestinal series showed that the stomach was unusually high and flexed on itself. The gastric rugae were rather prominent, and there was considerable spasm of the median portions of the stomach and of the pylorus. Peristalsis was irregular and at times quite active. There was a constant and characteristic clover leaf deformity of the duodenal bulb. The evidence of active spasm and by peristalsis was greater than that at an observation ten months previously.

The temperature, pulse and respirations remained normal throughout his hospital stay of nineteen days. During this time he received Sippy powders, with a supplementary dietary regimen, sedation, occasional parenteral fluids and bed rest, he was discharged improved.

Second Admission (two years later) The patient was readmitted complaining of vomiting and epigastric pain. He stated that for many months he had been increasingly annoyed with postprandial gaseous abdominal distention, bloating and belching. With the bloating which usually occurred about fifteen minutes after eating he developed severe mid-epigastric pain relieved only by purposefully vomiting the ingested food. These emeses happened from one to twelve times a day and were usually spontaneous, but he added that there were periods of a month or more when these complaints were absent. He also stated that he had been slightly dyspneic on moderate exertion and that his ankles had been questionably swollen on occasions. He had noted slight nocturia. The physical examination was unchanged from the first admission. Urinary examination showed an amber cloudy urine with a neutral reaction and a specific gravity of 1.009 on two occasions there was the slightest possible trace of albumin and occasional red and white blood cells. The blood showed a red-cell count of 3,800,000 with 65 per cent hemoglobin and a white-cell count of 8,700. The smear was normal. The vomitus was guaiac negative. A urinary concentration test showed specific gravities ranging from 1.005 to 1.009 and

1570 cc. excreted in twenty-four hours. Phenolsulfonephthalein kidney-function tests revealed a 22 per cent excretion at the end of two hours, with 6 per cent during the first fifteen minutes. The blood nonprotein nitrogen ranged from 92 to 78 mg per 100 cc. The serum protein was 6.9 gm per 100 cc, and the chlorides were equivalent to 100 cc of N/10 sodium chloride, the serum uric acid was 3.6 mg per 100 cc, the serum calcium 11.66 mg, the serum phosphorus 6.24 mg, and the carbon-dioxide combining power 65 and 48 vol per cent. X-ray films of the chest were negative. A gastrointestinal series showed a small pocket in the esophagus which filled with barium, located near the aortic arch. Gastric peristalsis was more vigorous than normal. There was some delay in the passage of barium from the stomach to the duodenum, and the latter showed a constant deformity of much the same character as that previously noted. However, spot films of the duodenal bulb showed no evidence of an ulcer crater. Intravenous pyelograms revealed kidney outlines which were about half normal size. The dye was secreted very slowly so that at no time were the kidney pelves or ureters sufficiently well filled to show their outlines distinctly, but they were apparently negative.

The patient's temperature, pulse and respirations were normal. He was treated in much the same way as at the time of his previous entry, and was discharged on the twenty-ninth hospital day.

Third Admission (six months later) He was readmitted complaining of great pain and tenderness over the flexor tendons of the right wrist. Pressure over these tendons caused excruciating pain, but movements of the hand without motion of these tendons caused no pain. He had first noted the difficulty on awakening in the middle of the night with his hand over his head, sudden flexion of the wrist had produced an excruciating pain which kept him awake day and night, in spite of rather heavy medication. It was further noted that the patient had experienced definite pain in the legs with exercise and that the pulsations in the right popliteal and posterior tibial arteries were faint, that of the dorsalis pedis artery almost impalpable. The laboratory and x-ray data were unchanged. The wrist and hand were splinted, and a plaster mould and gauntlet made, the patient was discharged home where the pain in his hand improved rapidly.

Fourth Admission (six months later) He was again readmitted because of several vomiting attacks following fatigue of physical or emotional origin. He had done "fairly well" since his last discharge until several days of vomiting had fol-

lowed the upsets associated with the installation of a telephone. He was dehydrated, oliguric and distended and had an acetone breath. He was given parenteral fluids. The serum nonprotein nitrogens successively were 98, 62 and 80 mg per 100 cc, and the serum chlorides were equivalent to 92, 96 and 100 cc. of N/10 sodium chloride. After slight improvement he was discharged on the sixth hospital day.

Fifth Admission (two and a half years later) This admission resulted from an acute upper respiratory infection of two days' duration, associated with an intense desire to urinate, and incontinence. He dribbled 60 to 90 cc of urine every one and a half hours. Examination showed a fairly marked coarse tremor of the hands, feet and tongue. There were dyspnea and orthopnea, and the chest was barrel shaped. The heart seemed to be slightly enlarged to the left and downward, the sounds were distant and of rather poor quality, the blood pressure was 160 systolic, 92 diastolic, and the pulse 112. The breath was definitely urinous. The prostate was slightly enlarged, round, solid and suspiciously hard on the right. The urine had a specific gravity of 1.004 and a + albumin, the sediment showed a rare red and 4 white blood cells per high power field. He was discharged relieved on the sixth hospital day.

Final Admission (six months later) Six years after the first recorded entry, the patient returned to the hospital. For one month prior to admission he had suffered with attacks of substernal pain, which were relieved with nitroglycerin and codeine. Twenty-four hours before entry the discomfort became severe and was unrelieved by medication. He also had experienced nausea, vomiting, belching and cough without sputum. His condition became critical, the blood pressure fell to 95 systolic, 60 diastolic. He quickly failed and died a few hours after hospitalization. An electrocardiogram taken before death showed a ventricular rate of 110, an inverted T₁, a sagging ST₂, an inverted T₄ and an upright T₃, with normal rhythm and moderate left-axis deviation.

DIFFERENTIAL DIAGNOSIS

DR. ALFRED KRANES I think we can be reasonably certain that when this patient first began to be ill he had a duodenal ulcer and that this accounted for his symptoms during the early part of his illness. That is borne out by the later x-ray evidence—although no crater was ever demonstrated—and also by the story that twelve years before entry he had had an attack of bleeding presumably from the ulcer, although we have

no objective evidence that he did bleed. The story then continues to record gastrointestinal symptoms, but they seem to change a bit in character. He began to have nausea, vomiting and gastric distress, lasting two days to a week. The implication is that they were on an emotional basis,—which they may very well have been,—but in view of what subsequently follows we have to take them more seriously and wonder if any new development had taken place which had changed his original gastrointestinal symptoms. Concerning the gastric analysis showing a free acid of 25 units, it would be important to know whether that was the height of the curve or whether it was a fasting specimen. If he had a free acid of only 25 units after alcohol and histamine, it would be some evidence that there was impairment of gastric function. It would be unusual, although it does occur with duodenal ulcer, to have so little hydrochloric acid present, and it makes you wonder whether there was something else which was depressing gastric secretion. Then he developed severe persistent vomiting attacks, during which he experienced a temporary psychosis and which recurred and led to his first hospital admission. At that time we have the first observations pointing toward renal insufficiency. He had an elevated nonprotein nitrogen and a fixed specific gravity of his urine. X ray study revealed a duodenal deformity without any evidence of an active crater. May we see the films, Dr. Schatzki?

DR. RICHARD SCHATZKI: The films show that he definitely had an old duodenal ulcer as far back as eight years preceding death. There was a clover leaf deformity of the cap apparently with an active ulcer at that time. In 1938 the last film also shows the clover leaf deformity of the cap and evidence of activity. This is the film taken in 1935; it shows a scar but no evidence of activity.

DR. KRANES: As I said, he showed evidence at that time of renal insufficiency. One might reasonably wonder, however, whether he had any structural changes in the kidney or whether the signs of renal insufficiency were the result of persistent vomiting or of administration of alkali. It is well known that people with peptic ulcers may develop uremia following vomiting, so-called achloremic uremia, and also as a result of the prolonged or intensive administration of alkalis. We are not told how much alkali he received.

DR. CHESTER M. JONES: He received tremendous amounts during the first portion of his treatment. He received none after 1935, when I first saw him. He had been treated for four years on routine ulcer medication with a great deal of alkali.

DR. KRANES: We can reasonably ask here then whether the administration of alkali may have depressed the renal function so that he went into uremia. Such cases have been reported. The exact mechanism is not quite clear, but it certainly occurs. It would have been of extreme interest at that time to have known the carbon-dioxide combining power. I think we can infer that the uremia was probably not due to vomiting, because the blood chlorides, although somewhat depressed, were not down in the range where achloremic uremia takes place (300 mg per 100 cc.). This transient psychosis may have been due to uremia. People with uremia do have psychoses. On the other hand it may have been a drug psychosis, the result of hypodermic medication in a vomiting patient with poor renal function and therefore faulty excretion of the drug. His improvement under Sippy powders, during his first admission, argues very much against alkalies as the cause of his renal insufficiency. If it was, he should have become worse. It begins to appear that his vomiting was probably uremic and not due to his ulcer, since he did not have pyloric obstruction by x ray study and the type of vomiting described is not that of pyloric obstruction. If this is true, alkaline therapy seems to have played no part in the renal picture, since the vomiting improved with the administration of Sippy powders.

There are several significant omissions in this record despite its length. I do not want to appear ungrateful for all this information but nevertheless in a patient with renal disease one is interested in certain specific things. The blood pressure is one, and there is scant mention of it throughout this long record. Anemia is another and there is only one red count, and one hemoglobin, recorded during the second admission. Furthermore, no examination of the fundi is recorded at any time.

DR. JONES: In 1935 examination of the fundi showed the vessels small in caliber but was otherwise not important. The blood pressure at that time was 130 systolic 80 diastolic.

DR. KRANES: On the second admission the blood pressure is not recorded. He continued to show signs of marked renal failure by all tests. There are some interesting blood chemical findings during this admission which are unusual in uncomplicated uremia. Three things strike me. The first is a uric acid of 3.6 mg per 100 cc., which is normal. With the marked nitrogen retention which this patient showed one would expect a much higher uric acid in the blood, I do not know why it should have been normal and can not explain it. The second is the carbon-dioxide combining power which was normal or slightly

above normal, whereas most patients with uremia develop an acidosis with a consequent lowering of the carbon-dioxide combining power. There are two possible explanations for this normal or slightly elevated reading: he may have been receiving large amounts of alkali, which would tend to keep it up, or he may have been vomiting quite a lot of chloride, which would have the same effect. However, if the latter were the case one would expect the blood chlorides to be low. Since they are reported to be normal, the administration of alkali probably explains the normal level. The third point is the serum calcium of 11.6 mg per 100 cc. This in a healthy person might be considered normal or perhaps at the upper limit of normal. However, in a patient with renal failure it is definitely abnormal, particularly with a serum phosphorus of 6.24 mg per 100 cc. Uremic patients usually have a low blood calcium, about 6 to 9 mg as a rule, whereas this is quite above what one would expect. It makes one wonder about two possibilities. Could this patient with prolonged renal insufficiency have developed secondary parathyroid hyperplasia? Although there is no other proof that the parathyroid glands were involved, it is the most probable explanation. Could this patient possibly have had a "myeloma" kidney? Elevated serum calciums are not uncommon in cases of multiple myeloma, with or without renal insufficiency. However there is not the slightest evidence of this.

What the acute process in the right wrist was, I do not know. There is no examination recorded of the wrist, and I have no idea what it was. It reminds me of one patient that was studied here extensively several years ago, a patient with prolonged renal insufficiency, who developed metastatic areas of calcification near various joints and tendons which were quite painful. That patient also had a marked secondary hyperparathyroidism as a result of renal failure, and it is quite conceivable that this acute wrist represents some such phenomenon — metastatic calcification in a tendon. Six months later he was again admitted with another episode of renal failure, and improved.

Finally six months before his last admission we have the first evidence that there may have been something wrong with the prostate, although nothing more is said about it and we are left high and dry as to whether the prostate was enlarged or whether there was any real evidence of cancer. I shall disregard it, since nothing further is said about it. One would also like to know what happened to the dribbling or incontinence, whether it was a temporary affair or lasted any length of time. I am inclined to believe it was temporary because no further mention is made of it. On this admission we have the first recorded evidence that

his blood pressure had become elevated — 160 systolic, 92 diastolic. Previous to that it had apparently been normal. He finally was admitted with an episode which I take to be fairly characteristic of coronary thrombosis and which proved fatal.

So far as the gastrointestinal lesion goes, I think he probably had a healed duodenal ulcer, active many years before but healing during the latter part of his life, possibly the result of the lowered chloride secretion that occurs in the stomachs of patients who develop uremia. At any rate, I do not believe it played much of a role in his death or in the major part of his illness. He must have had something else going on in the gastrointestinal tract, probably in the nature of a uremic gastritis. Are there any more films that might help?

DR SCHATZKI: The films show no evidence of gastritis. That does not exclude the presence of gastritis.

DR KRANES: Patients with uremia often develop gastrointestinal lesions, anywhere from the mouth to the anus. They excrete urea in the gastrointestinal tract and ammonia forms producing severe irritation of the mucous membrane.

So far as the renal situation goes, I am inclined to believe that this patient had some structural changes in the kidneys. There are several things that stand out in the renal story, the first is the duration. We know he had been in renal failure for eight years, and probably longer. The second is the essentially normal urine, except for the fixed specific gravity — no albumin and a negative sediment. The absence of hypertension, except toward the end, is another significant and unusual finding. Just what type of renal disease this patient had, I am sure I do not know. There is nothing in this story or in the past history that gives us any clue as to the type of renal disease that was going on. On a purely statistical basis I think chronic glomerulonephritis would probably be the most likely diagnosis. Another possibility is a chronic pyelonephritis or a healed pyelonephritis. There is no evidence from the history of either one, but both are possible. I think we also have to keep in mind the possibility that this man had "myeloma" kidneys, but of this there is no evidence. Are there any x-ray films of the bones?

DR SCHATZKI: In regard to the "myeloma" kidney, he had kidneys that were definitely smaller than is normal for a man of his size. They are, at most, half the size they ought to be. At that time he had very poor concentration.

DR KRANES: With kidneys as small as that one can fairly safely exclude myeloma. I think the safest thing to say is that this patient had nephritis. I shall leave it up to Dr. Mallory to tell us whether it was chronic glomerulonephritis.

pyelonephritis or possibly some other type which we have not mentioned. Whether his prostate played any role, I do not know, but I rather think not. There is not much evidence of chronic prostatism in this patient. I should also guess that he had a fairly good degree of parathyroid hyperplasia and that the terminal illness was most likely coronary thrombosis.

Dr. JONES: This story is a long one, and even at its present length it did not include certain things that are of interest but do not affect the diagnosis so far as Dr. Krane's is concerned. It represents the life history of several diseases. I saw this man in 1935 at the request of Dr. John Taylor who had followed him as a duodenal ulcer patient for several years. Up to that time the diagnoses had been ulcer and psychoneurosis. He was one of the most mercurial individuals I have ever seen. Under any pressure or disturbance he developed gastrointestinal symptoms. He did not tolerate alkalis very well and in 1935 he showed for the first time the picture of alkalosis. On one occasion a few months later while being given calcium carbonate, which ordinarily does not produce much trouble, he developed an alkalosis which was mild in degree but definite so far as the blood chemistry was concerned. The calcium carbonate was eliminated and he had no further trouble from the point of view of this renal disturbance. The first study of the urine was in 1931, four years before I first saw him, and this showed a concentration of 1028, with no albumin. In 1931 he had no obvious evidence of nephritis. From 1932 on the specific gravity never went higher than 1016. In 1935 the first studies that I was able to do on him showed that he had a specific gravity ranging from 1010 to 1014. His output was 1465 cc during the day and 1570 cc. at night. The quantity of night urine was increased over the day urine for the four years before death. From then on, and even at that time, he showed all the chemical findings one could desire of renal insufficiency and a breath which was strongly uremic. It was not urinous. It was the breath of one with nitrogen retention. I remember that one morning I called Dr. Walter Bauer into the office to make a diagnosis. He smelled this man's breath and said "He has nephritis and is in uremia." That persisted for five years. The blood creatinin was 5.6 mg per 100 cc., which is high. Ordinarily one expects to find the patient seriously ill with as high a creatinin as that. The urinary picture was marked, as he went along with increasing frequency and nocturia. At no time did he have any evidence of inability to handle himself. He was a fairly normal person up to

within a few weeks of death. He was ambulatory and went to California six weeks before death and aside from some unpleasant attacks of circulatory disturbance on the trip, he got along perfectly well. In 1936 he began to complain of very slight substernal oppression on exertion. One year before death he complained because he was unable to swim a quarter of a mile. He carried out vigorous exercise before death. Until six months before death he was able to swim 100 yards in fairly cold water with only a little subsequent substernal oppression. At the end of 1938 he had definite attacks of intermittent claudication in both legs. He could walk only so far and then had to stop for a while, but it did not prevent his going. He just stopped and rested. The pain in the wrist was diagnosed as tenosynovitis. It is possible he had some calcium in the tendon sheath at that time. In the last year of his life he had symptoms of rather characteristic repeated anginal attacks, finally leading to an absolutely characteristic attack of coronary thrombosis. He walked into the office and said "I have something serious the matter with my heart." He died thirty six hours later.

CLINICAL DIAGNOSES

Coronary infarction
Chronic nephritis, with arteriosclerosis
Duodenal ulcer

DR. KRANE'S DIAGNOSES

Duodenal ulcer, healed.
Chronic nephritis
Glomerulonephritis?
Pyelonephritis?
Parathyroid hyperplasia
Coronary thrombosis.

ANATOMICAL DIAGNOSES

Duodenal and pyloric ulcer, slightly active
Healed pyelonephritis.
Parathyroid hyperplasia
Coronary sclerosis, with thrombosis
Calcification of annulus fibrosus of mitral valve, early

PATHOLOGICAL DISCUSSION

Dr. Tracy B. Mallory: As you gathered from the clinical story this is a most unusual case and I do not believe I can do as well with the pathology as the clinicians have done. I can confirm all that they have said. The final cause of death was coronary thrombosis. We found nearly all

the coronary vessels occluded, some chronically and some acutely. The kidneys were extremely small, weighing only 100 gm. There was a very marked secondary hyperplasia of the parathyroid glands, and there was a duodenal ulcer which spread across the pyloric ring, slightly into the stomach, showing at least some degree of activity. There are, however, a great many things that are more difficult to explain. First, is the question of what type of kidney disease we have here. We often get a good deal of help from the gross appearance of the kidneys. I should say we got none in this case because the kidneys had a great many of the retention cysts that one sees in elderly people, and the gross shape of the kidneys was so distorted by the cysts that it was impossible to make out what it might have been. Microscopically, they showed a disproportionately high destruction of tubules, a relative maintenance of glomeruli and a considerable degree of lymphocytic infiltration, perhaps a little more than the average chronic nephritis would show. There are one or two tubules that contain a few leukocytes, but certainly nowhere is there abscess formation or anything that could be considered active pyelonephritis. The tubules contained an unusually large number of casts. On the whole, the findings are those that are usually considered characteristic of a chronic or burnt-out pyelonephritis. We have recently had our attention called to that condition as a frequent cause for what seems clinically to be essential hypertension. It is interesting to note that this man had so little evidence of hypertension, even at the very end. With the prolonged renal insufficiency, virtually amounting to six years of uremia, it was inevitable that the parathyroid glands would be enlarged. We did not actually weigh them, but from the measurements we can assume about 2 gm of parathyroid tissue, which is a tenfold increase above the normal. On the other hand, every case we have seen heretofore with marked secondary hyperplasia of the parathyroid glands has shown evident osteitis fibrosa on microscopic examination even if it was not evident by x-ray during life.

A PHYSICIAN: Did the diet have anything to do with it?

DR MALLORY: It seems possible, and I have no other explanation to offer.

There was a final anatomical finding which I cannot explain—an area of what seemed to be caseous necrosis in the myocardium high up in the ventricular wall and just underneath the mitral ring, which was partially calcified. It was fairly circumscribed, measuring about 25 by 10 cm. From time to time we see cases with a very marked calcification of the annulus fibrosus of the mitral

ring, both with and without evidence of myocardial involvement. This man showed a complete calcified vegetation on the mitral valve, as well as partial calcification of the myocardium. Whether it represents an early stage of the syndrome of calcification of the annulus fibrosus, I do not know, and I have no idea what might give it. It may, of course, have been merely a focus of metastatic calcification such as occurs often in the syndrome of renal rickets, but the absence of any other focus of calcification makes it seem improbable.

CASE 25502

PRESENTATION OF CASE

A seventy-year-old, Italian-born, American laborer was admitted to the hospital complaining of epigastric pain.

The patient was well until ten months before admission when he began having four-hour attacks of epigastric pain which "came and went," accentuated by heavy meals. The pain was not constant but at times was severe enough to prevent him from eating. Occasionally there was associated nausea, but no vomiting. He was seen by the Out Patient Department nine months before admission, where gastrointestinal x-ray studies showed a normal esophagus, stomach and duodenum. He was placed on a normal diet with a tablespoonful of mineral oil daily, and was discharged without a definitely established diagnosis. Eight months before admission he was again seen in the Out Patient Department and stated that he was not improved. Six months before entry, however, his patient's family noticed that he was losing weight. Apparently his appetite had been poor because of a subjective fear of producing epigastric pain with eating. Three months before admission he began having almost weekly attacks of fever lasting one or two days. With one of the fevers, six weeks before entry, he was seen by an outside physician, who referred the patient to another hospital where he remained about four weeks. While there he was studied for the still persistent recurrent epigastric pain. A few days later he became jaundiced, but gradually the pain disappeared and he felt no further steady discomfort. The jaundice waxed and waned as the patient became increasingly pale. He suffered two more severe chills during this period of hospitalization, but for some undetermined reason he was discharged home where he remained until his admission to this institution. Two days before admission he developed severe shaking chills with profuse sweating, white stools and deepening jaundice; he felt weak, was anorexic and had another attack of fever and chills on the day of admission. He had

a great deal of weight during the present illness. The past, family and marital histories were not contributory.

Physical examination revealed an emaciated, deeply jaundiced, feverish man who had a severe shaking chill during the examination. The skin was hot and dry, and both skin and sclerae were icteric. The oral and pharyngeal mucous membranes were dry, and the throat was covered with a thick tenacious exudate. The heart was enlarged 15 cm beyond the midclavicular line in the fifth interspace. There was a soft blowing apical systolic murmur, the rate was 110, with regular rhythm. The blood pressure was 136 systolic, 80 diastolic, and there was "moderate peripheral arteriosclerosis." The lungs showed dullness at the right base, with subcrepitant inspiratory rales in the right axilla. The abdomen was flat, with voluntary spasm in the upper quadrant but no tenderness. A small palpable mass in the right upper quadrant was found to descend below the costal margin on deep inspiration and was thought by the examiner to have been the gall bladder. The left lobe of the liver was enlarged and filled the upper half of the epigastrium. There were no other positive findings.

The temperature was 103°F., the pulse 110, and the respirations 30.

The urine examination showed a + bile test, and there were 2 to 4 white blood cells per high power field in the sediment. The blood showed a red-cell count of 3,100,000 with 70 per cent hemoglobin (Tallqvist), and a white-cell count of 17,000. The red cells were microcytic and hypochromic. The hematocrit was 31.5 per cent, and the plasma prothrombin 40.9 per cent normal. A bromsulphalein test showed 100 per cent retention; the van den Berg was 20 mg. bilirubin direct, the hippuric acid 1.7 gm and the plasma creatinine 0.44 mg per 100 cc. The blood serum cholesterol was 39 mg., the nonprotein nitrogen 20 mg., and the serum protein 5.7 gm per 100 cc., the serum chlorides were equivalent to 101.9 cc. of N/10 sodium chloride, and the carbon-dioxide combining power to 19 cc of N/10 carbonic acid.

X-ray studies of the chest revealed a normal sized heart, a tortuous and calcified aorta and increased lung markings. There was no definite evidence of metastases or pneumonia. Films of the pelvis and lumbar spine showed moderate hypertrophic changes, with marked osteoporosis but no evidence of metastases.

The patient ran a short, downhill course with spiking temperature (97 to 103°F.), rapid pulse (100 to 130) and rapid respirations (20 to 40). On the third day his white blood-cell count was 21,600 with 94 per cent polymorphonuclears. The

dehydration was difficult to combat. He became irrational and stuporous and developed ankle edema. A large, tender liver was palpated, but there was no evidence of ascites. Dullness with decreased breath sounds was noted at the right base. He failed rapidly and died on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD H. SWEET: The reports of the x-ray studies seem to indicate that the films were negative. Is there any comment to make about them? No mention is made of a Graham test.

DR. RICHARD SCHATZKI: Examination of the upper gastrointestinal tract nine months before admission showed a normal stomach and duodenum with the exception of a small diverticulum in the region of the papilla of Vater. The next examination is a flat abdominal film taken at the time of admission. It shows some osteoporosis but not more than one would expect in a patient of his age. There are arteriosclerotic and degenerative changes but nothing that would help with the diagnosis. This is a calcified mesenteric node. There is no special flat film of the gall-bladder region. The only film is one taken with the patient face up and in it I cannot see any stones in the region of the gall bladder. The other film is one of the chest, apparently taken at that admission, as the patient was lying down; it is not a six foot film, probably four or five feet and I refrain from making a statement regarding the size of the heart. The lung markings are increased as if he might have been slightly decompensated. The lung markings are, however, not very definite.

DR. SWEET: We get little information of value from the x-ray studies, except negative evidence. It is obvious after reviewing this case that we are dealing with a history starting rather vaguely and ending up with a definite case of so-called "Charcot's intermittent hepatic fever," which we know is usually superimposed on some type of biliary tract obstruction. Whether such obstruction is due to stone, stricture or carcinoma is not always possible to say. Of course in our clinical experience the number of cases with stone in the duct is greater than that of those with carcinoma so we are apt to have the impression that with this syndrome we should consider carcinoma only rarely. When I started to think about the case that was my first impression, but I am not sure that it is correct. Therefore, let us try by a careful analysis of the symptoms and findings to decide on what basis this case of intermittent hepatic fever rests.

First of all this patient with a life-long history of apparently good health, began at the age of seventy to suffer pain, which is one of the most important symptoms to analyze in any case history. I get the impression, however, that it was never a severe lancinating type of pain such as one often hears about in cases with stone. It is described as dull, accentuated by meals and located in the epigastrium, it apparently did not radiate, and once or twice it is referred to as "distress." There is very little mention of it in the history. Could it have been due to stone or to carcinoma? We think of those with carcinoma as not having pain. That is usually true with carcinoma of the pancreas, but with carcinoma in the ducts, pain of this type may very well occur. On the other hand, one need not have severe pain in cases with stone, and in fact such patients often complain only of distress and a vague feeling of discomfort. Occasionally there is a stone in the ducts without any pain.

The jaundice began later—eight months after onset. It is said to have fluctuated, but that is apt to be an unreliable observation. It certainly tended to be progressive and became very severe, judging from the way the history is worded. We know that a sizable percentage of cases with stone in the common duct may occur without jaundice—Dr. Daniel F. Jones used to put it at about 40 per cent of all cases, but we also know that in cases in which the obstruction is due to progressive stricture, caused either by pancreatitis or by malignant disease, jaundice, while it may later be intermittent and allow some bile to go through into the stools, tends to be progressive and to become severe. So from the type and nature of the jaundice in this case one guesses that it was due to carcinoma rather than to stone.

Nausea is not mentioned as a prominent symptom, and I have the impression from my observation of patients that gallstones do not ordinarily produce much nausea. I should expect, however, that if the patient had carcinoma of the pancreas or some such condition there would have been more nausea. When the liver is invaded with carcinoma, it is often a predominant symptom. The anorexia might go with either condition, but it is described here as being due to fear of pain, in other words, fear to eat because he might have pain as a result. Later, with the jaundice and the evidence of liver obstruction and enlargement, anorexia might very well have been due to liver damage. The fever and chills, occurring in attacks with remissions and coming after the jaundice had become manifest, represent a good clinical description of the Charcot syndrome. So if we were to confine our analysis to a review of the

history, I think we should have to say that the obstruction might be due to stone or to carcinoma. I have somehow the impression that it is due to both.

So far as the physical examination goes, we note first of all that there was marked emaciation, which was an early sign. That may have been due to anorexia or fear of eating, but it was severe and progressive and it may well have meant that he had malignant disease rather than stone. We must remember that this patient was well, we assume, until he reached the age of seventy, and then over the course of ten months he steadily lost weight. He had constant anorexia and repeated attacks of pain, and later, fever and chills. In other words, the disease was progressive. My impression is that if it had been entirely due to stone there would have been periods when he was relatively well, although I admit that he could have died of a stone that obstructed the common duct, with superimposed infection in the biliary tract. The jaundice we have talked about. The stools eventually became acholic, and stayed so. The usual signs of fever, dry skin and so forth were obvious and need not enter into the discussion. The dullness and rales in the chest suggest that he might have had pneumonia. This was not borne out by x-ray study, and that is a common experience.

We then come to the questionable mass in the region of the gall bladder. I should assume from the description that the gall bladder was felt, on the other hand it is described as small. We are accustomed, as you know, to feeling a large, distended gall bladder in cases with obstruction of the common bile duct due to carcinoma of the pancreas, according to Courvoisier's law. But that need not be so, and although I do not believe he had carcinoma of the pancreas we need not rule it out on that basis or rule it in either. The gall bladder was felt, however. The other important physical finding was the asymmetrical enlargement of the liver. The record mentions an enlarged left lobe, but nothing is said of the right, this suggests to me that there was some malignant process in the liver itself during the end of his illness.

One can sum up the laboratory findings by saying that they tell us chiefly that he had anemia, obstructive jaundice, diminished liver function and acidosis. We have commented on the x-ray studies. The course in the hospital is obvious and to be expected.

What did this patient have? We know that he had infection of the biliary tract, but what was the underlying lesion? I have covered in the discussion most of the essential points. The physical

examination toward the end of his life suggests to me that he had at that time a carcinoma of the liver. The knowledge that carcinoma of the liver is exceedingly rare as a primary disease and more often dependent on disease in the duct system of the liver or gall bladder or some adjacent viscus and the matter also of the questionably palpable gall bladder which was not particularly large, all enter into the consideration of the diagnosis. I suggest that this man had carcinoma of the biliary system, invading the liver perhaps originating in the gall bladder and therefore, perhaps in a gall bladder that contained stones, because we know that carcinoma of the gall bladder is commonly associated with gallstones. We also know that gallstones are quite common without the occurrence of carcinoma. To sum up, I believe there was infection of the liver and obstruction of the common duct. I cannot say for sure whether the obstruction was due to stone or carcinoma, but I think he had malignant disease, as I have described, and possibly stones as well. His long life without any symptoms is certainly against stones, in spite of the fact that we have all seen patients with stones who have gone through life without any symptoms.

CLINICAL DIAGNOSES

Carcinoma of head of pancreas, with obstructive jaundice.
Pneumonia, right lower lobe

DR. SWEET'S DIAGNOSES

Carcinoma of gall bladder with invasion of the bile ducts and liver
Cholelithiasis?

ANATOMICAL DIAGNOSES

Carcinoma of gall bladder, with invasion of liver and colon and obstruction of bile ducts and portal vein
Cholecystocolic fistula
Splenomegaly
Icterus
Ectopic pancreas surrounding duodenum

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY. The autopsy showed carcinoma and I think Dr. Sweet was right in placing the primary source in the gall bladder. It forms the only apparent exception, that I can remember in our series here, to the rule that carcinoma of the gall bladder is always associated with demonstrable gallstones. We could not find a gall stone, but there was a good reason for it because he had a fistula between the gall bladder and the colon, a rather wide one through which, without question, even a large gallstone could pass and probably had passed into the colon. The tumor had invaded widely into the bed of the gall bladder and throughout the right lobe of the liver. There were only two nodules in the left lobe. The liver was not strikingly enlarged, and I think what was felt and interpreted as the left lobe was the spleen, which was big, weighing about 500 gm. Enlargement of the spleen is quite unusual in cases of primary carcinoma of the biliary-duct system. The explanation for it in this case appeared to be that the tumor had grown down into the gastrohepatic ligament, had completely destroyed and obliterated both hepatic ducts and had grown about the portal vein to such an extent that it is reasonably certain it was causing a significant degree of obstruction.

One anatomic finding was a little unusual. The second portion of the duodenum was almost completely encircled by an ectopic pancreas. It was normal pancreatic tissue, however, not tumor, and I doubt if it played any part in his symptomatology.

DR. GRANTLEY W. TAYLOR. Could the long standing fever and apparent Charcot's syndrome have been due to infection?

DR. MALLORY. In some of the sections of the liver there were focal abscesses, and whether the fever should be explained on the basis of sepsis which had spread through the cholecystocolic fistula or was truly of the Charcot type due to extensive carcinoma within the liver I cannot say. Certainly both were present.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
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MATERIAL for early publication should be received not later than noon on Saturday

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COMMUNICATIONS should be addressed to the *New England Journal of Medicine* 8 Fenway Boston Massachusetts

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

THE Board of Trustees of the American Medical Association has recently formulated a set of proposals,—a so-called "Platform of the American Medical Association,"—which embodies in a reasonable and practical way many of the suggestions and recommendations relative to the problems concerning the health and medical care of the people of the United States which have been made by the House of Delegates in the past several years. Although this cannot strictly be termed "the platform" until officially adopted at the next session of the House of Delegates, it so closely conforms to the proposals sponsored by the latter that little doubt can be entertained as to its eventual acceptance.

The platform is as follows

1 The establishment of an agency of the federal government under which shall be co-ordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy

2 The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need

3 The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5 The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration

6 In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established

7 The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability

8 Expansion of public health and medical services consistent with the American system of democracy

The several points brought out in the platform refer to nothing that is new, but they do serve to express, in succinct form, the principles which have been, and still are, advocated by the Association. Furthermore, they represent constructive suggestions, with no hint of the attitude of destructive criticism for which the Association has been censured in the last two years.

The platform advocates a single federal agency for medical and health functions. It approves the granting of federal funds to the states for promoting such functions, provided there is proof of need. It emphasizes that the expansion of preventive medicine and the provision of care for the indigent and medically indigent are local problems and that existing qualified medical and hospital facilities should be considered in any proposed extension of service. It recognizes the need for increased avail-

ality of medical services, but warns that the private practice of medicine should continue, that the present quality of medical care should be maintained and that any expansion should be consistent with the American system of democracy.

Whether the solons in Washington will attempt to revise pending legislation in such a way as to conform to the principles set forth in this platform remains to be seen. The recommendations advanced at the National Health Conference in 1938 and the proposed Wagner Bill indicate that the governmental authorities have preconceived, though possibly alterable, ideas in regard to the requirements of proper health legislation. If this is true, there is all the more need for bringing this practical, though somewhat belated, platform to the attention of those individuals in Washington who are responsible for the drafting and enactment of laws relative to the health and medical care of the people of the United States.

PSYCHOSOMATIC MEDICINE

In recent years there has been a growth of interest in psychosomatic medical problems and research is going forward in this line of endeavor. It is not surprising, therefore, that a special journal, *Psychosomatic Medicine*, has been started to publish papers on the psychological aspects of medicine, as well as on experimental studies of various types. It is to be published quarterly, under the sponsorship of the Committee on Problems of Neurotic Behavior, Division of Anthropology and Psychology, National Research Council, Washington, District of Columbia. The first number was issued in January, 1939, and contains a statement of the aims of the editors, which is to encourage and bring together studies contributing to the understanding of the organism as a whole. Recent studies of emotional factors in the etiology and the course of organic illness have demonstrated that the scientific method is as essential to satisfactory management of patients with psychoses as it is to that of individuals showing somatic aspects of dysfunction. The first issue of the journal considers some of these problems. Three papers are

given over to a discussion of the functions of the hypothalamus, and there follows a symposium of seven papers devoted to the subject of hypertension. *Psychosomatic Medicine* is a valuable addition to the field, and if the first number can be used as a guide, one expects that the journal will be of value to the medical profession.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D. *Secretary*
330 Dartmouth Street
Boston

PUERPERAL INFECTION FOLLOWING NORMAL DELIVERY

Mrs. L. T., a thirty-four year-old woman was admitted to the hospital on September 30, 1927, complaining of fluctuating fever, — which was highest in the evening — backache, and pain and tenderness in the lower abdomen. On September 7, 1927 the patient's eleventh child had been delivered uneventfully at home. On the second postpartum day she experienced a sudden, severe headache and a chill. Her temperature while at home had varied from 99 to 103°F. She had remained in bed and had received symptomatic treatment from the attending physician. During this time she had had considerable hypogastric tenderness on deep pressure. The lochia had been serosanguineous for two weeks, then it had changed to a thick yellowish discharge of moderate amount.

The family history was non-contributory. The patient had had the usual children's diseases. In 1915 the patient had had an "abscessed tube" following childbirth, and in 1926 a cholecystectomy. She had had one miscarriage. Catamenia began at twelve, were regular with a twenty-eight-day cycle and lasted three to four days with no pain.

On examination at entry the patient seemed to be in fairly good condition. She was rational and felt quite comfortable. The temperature was 103°F., the pulse 96, and the respirations 20. Her head and neck were essentially negative. The thorax, heart and lungs were also normal. The abdomen was soft and flabby with marked tenderness throughout the hypogastrium. There was an operative scar in the right upper quadrant. The extremities showed moderate varicosities and nor-

A series of selected case histories by members of the section will be published weekly. Comments and questions by members are solicited and will be discussed by members of the section.

mal reflexes. The blood showed a white-cell count of 9600 and a hemoglobin of 55 per cent. The urine contained many pus cells. A diagnosis of puerperal sepsis was made.

The treatment of the slight cough and abdominal pain was largely symptomatic. The patient received Creolin douches twice a day, with ice to the lower abdomen intermittently. Progress was essentially uneventful. Throughout her hospital stay her backache remained practically constant. She had a persistent dry cough and varying amounts of pelvic pain. Her temperature was of the picket-fence, septic type.

On October 10, vaginal examination disclosed a subinvolved, retroverted uterus with old cervical lacerations. No masses were found, and the tenderness was moderate. On October 23 a pelvic examination showed some induration at the base of the left broad ligament, but no definite masses. By November 6 a palpable mass had developed in the left lower quadrant.

The patient's temperature during the first four days ranged from 100 to 103°F. During the next eleven days it remained between 100 and 102°F, coming down to normal for the following three days. For the next five weeks the temperature fluctuated between 98 and 103.6°F, finally reaching normal on November 14, with a slight rise on November 18 when the patient got out of bed. From then on the chart was normal, and she was discharged on November 23, recovered.

A blood culture taken on October 24 showed *Staphylococcus albus*. The white-cell count varied between 9000 and 12,000, the red-cell count remained at about 3,500,000, and the hemoglobin ranged between 55 and 65 per cent. The urine continued to show many pus cells.

Comment. This case represents the characteristic course of puerperal infection resulting in parametric involvement. The onset, accompanied by a chill, occurred within thirty-six hours of a normal delivery. The treatment was entirely conservative. There is no note as to a vaginal examination at the time of entry, and in the absence of definite signs of pelvic involvement by masses or induration, the use of any kind of douche is open to question. On the other hand when there is definite evidence of pelvic involvement, copious hot douches given under low pressure are considered of value.

Blood examination revealed a moderate anemia. In cases of sepsis with accompanying anemia small transfusions are very often valuable. The positive blood culture of *Staphylococcus albus* showed that treatment should be entirely conservative. No known treatment has any specific effect on this organism, and the growth may well have been

due to contamination. Puerperal infection, most infections, will usually subside if treated symptomatically and conservatively.

MEDICAL POSTGRADUATE EXTENSION COURSES

The following sessions of the Medical Postgraduate Extension Courses have been arranged for the week beginning December 18.

BRISTOL NORTH

Thursday, December 21, at 4 00 p.m., at the Memorial Hospital, Taunton. Gonorrhea in the Female. Instructor Alonzo K. Paine. Lester E. Lester, *Chairman*.

ESSEX SOUTH

Tuesday, December 19, at 4 00 p.m., in the Conference Room of the Salem Hospital, Salem. Fractures and Spine Injuries. Instructor Donald M. J. Robert Shaughnessy, *Chairman*.

MIDDLESEX EAST

Tuesday, December 19, at 4 00 p.m., at the Memorial Hospital, Melrose. Complications in Obstetrics. Illustrated by case histories. Instructor J. C. Janney. Walter H. Flanders, *Chairman*.

WORCESTER (Milford Section)

Tuesday, December 19, at 8 30 p.m., in the Nurses' Home of the Milford Hospital, Milford. Pelvic Infection. Instructor Donald S. King. Joseph Ashkins, *Chairman*.

WORCESTER NORTH

Friday, December 22, at 4 30 p.m., in the Nurses' Home of the Burbank Hospital, Fitchburg. The Use of Drugs in the Treatment of Childbirth Infections. Instructor James M. Baty. George P. Keaveny, *Chairman*.

ANNUAL PRIZE FOR INTERNS

The attention of interns in Massachusetts hospitals is called to the fact that a prize of \$50.00 has been offered by the Massachusetts Medical Society for the best written and most comprehensive case report submitted by one of their number holding an internship in any Massachusetts hospital which is approved by the American Medical Association for intern training during 1938-1940.

This report is to be typewritten, and when complete is to be sealed, unsigned, in a plain envelope, which in turn is to be placed together with a separate slip bearing the name and address of the contestant, in a larger envelope, and sent to Committee on Medical Education and Medical Diplomas, Massachusetts Medical Society, 8 Fenway, Boston.

The contest this year closes May 5, 1940. Reports may be submitted at any time prior to that date.

DEATHS

BURKE—JAMES J. BURKE, M.D., of Easthampton, died November 16. He was in his eightieth year. Born in Chicopee, he attended the Holy Name School and Holy Cross College. He received his degree from Bellevue Hospital Medical College in 1885. He was a member of the Massachusetts Medical Society and the American Medical Association. Dr. Burke married Mary A. Powers who died in 1930. There were no children.

DAMSKY—**CHARLES DAMSKY, M.D.**, of Lynn died November 3. He was in his forty-sixth year. Dr. Damsky received his degree from the Middlesex College of Medicine and Surgery in 1921 and studied in Paris, Italy and England. He had practiced in Lynn fifteen years, and was chief orthopedic surgeon at the City Hospital. He was a fellow of the Massachusetts Medical Society and the American Medical Association. His widow, two sons, a brother and six sisters survive.

HUGHES—**FRANK HUGHES, M.D.**, of Dorchester died November 13. He was in his sixty-eighth year. Dr. Hughes was born in Sussex, England. He received his degree from Tufts College Medical School in 1910 and held memberships in the Massachusetts Medical Society and the American Medical Association. His widow and a daughter survive him.

ISCELLANY

NOTES

Harvard University has recently announced the promotion at Harvard Medical School of Dr. C. Guy Lane to clinical professor of dermatology and that of Dr. Francis R. Curran to associate professor of medicine.

The trustees of Middlesex University have recently announced the appointment of Dr. John Hall Smith as dean of the School of Medicine. Dr. William M. Konikow who has been serving both as dean and as professor of anatomy found that the duties of both positions made it impossible to devote his full energies in a teaching capacity. Dr. Smith received his medical degree from the Louisville Medical College in 1896 and has practiced surgery in Boston since 1898. He is a member of the Massachusetts Medical Society and a fellow of the American Medical Association. He has been actively engaged in medical education for over twenty-five years and retired from practice some ten years ago to devote his entire time to the administrative affairs of Middlesex University. At the time of his appointment as dean Dr. Smith was professor of anatomy and of clinical surgery on the medical faculty. He designed and supervised the construction of the new group of medical buildings on the university campus and the erection of this medical group was made possible through substantial funds donated by Dr. Smith over a period of years.

The trustees have appointed Dr. David L. Davidson, professor of biochemistry, as assistant to the dean.

CORRESPONDENCE

ASSAULT OF BAD CHECKS

To the Editor—Dr. Herbert C. Kimberlin, of Trenton, Missouri has requested the co-operation of this department in warning oculists against a man who is passing bad checks. The checks are drawn to an amount exceeding the cost of the glasses, and the difference is received in cash from the oculist. Working north and east from Missouri, the man was last heard of in New York State. His description is given in the following letter written to Dr. C. M. Sneed of Columbia Missouri. Unfortunately the check-passer reached Dr. Sneed before the letter did, costing Dr. Sneed \$150.00.

I am writing you regarding a man who is running around the country buying glasses especially from oculists, and usually giving a check to the amount of \$30.00. This man tries to stimulate a farmer and he usually has a notion on the check to him for corn, a cow, hogs and so forth. The name on the check to him is no doubt forged and there is no doubt that his endorsement on the back of the check is forged. The man is about five feet ten inches tall, weighs about 155 pounds, has light sandy hair and blue eyes and is smooth shaven, with a ruddy complexion, and about forty-nine years old.

Should a man come into your office making an attempt to cash a check as described above, unless proved to be absolutely authentic, please notify Sheriff of Grundy County, Trenton, Missouri.

He usually signs his name on the back of the check in a very rough but plainly legible hand and signs it W. C. Curran. He usually wishes the difference between the amount of the check and the price of the glasses in cash, but does not call for the glasses. Should he sign his name and such a check be presented to you, please have the sheriff intercept him.

Should you have any information regarding a man of his description passing checks of the above description, please inform the sheriff above named, Dr. R. C. Pearson, Maryville, Missouri or myself.

We have further information to the effect that the wanted man has passed checks bearing the name of J. B. Powers, W. C. Cursey and J. C. Gardner. He was using the latter name at the time he was in Olean, New York.

PAUL J. JAKOWITZ, M.D.,
Commissioner of Public Health

State House,
Boston.

HARVEY CUSHING AND BOOKS

To the Editor—Dr. Harvey Cushing loved books. He wrote once "Books are the most important tools of our craft." He loved to read them. We were told recently in a resolution relative to his death that "books and journals flowed freely and at times, almost weekly" from the Boston Medical Library to the hospital where he worked, carried away in armfuls by the "faithful Gus."

Dr. Cushing loved not only to read books, but also to own them. He was a great collector of Americana. And his library so rich in early American medical works, medical incunabula and so forth was always open to the research worker and the bibliophile. In that connection, I should like to relate—and it is the purpose of this letter—an incident which might be of interest for the light it throws upon the personality of Dr. Cushing.

A few years ago, after receiving a catalogue from a certain bookdealer, I sent an order for a rather rare item—Schoepf's *The Climate and Diseases of America*—only to find out that Dr. Cushing had been an earlier bird and had gotten the worm. To my surprise a few days later I received the book from Dr. Cushing with a note telling me that he was sorry to have been ahead of me in the purchase of the book and that he was sending it to me for my own perusal. I was a complete stranger to him and yet he was sending me that precious little volume before having had a chance to read it himself!

John Shaw Billings did the same thing once for Oler, lending him a rare book. And Oler left it on the train from Washington to Baltimore and it was never recovered.

How many collectors would have done what Cushing did? I know I would not.

GABRIEL NADEAU

Rutland State Sanatorium,
Rutland, Massachusetts

NOTICES

REMOVAL

SAMUEL ORLOV, MD, announces the removal of his office to 341 Main Street, Wareham

RESULTS OF JULY BOARD EXAMINATIONS

To the Editor I am enclosing a statement of the results of the July, 1939, examination conducted by the Board of Registration in Medicine.

STEPHEN RUSHMORE, MD, Secretary

State House, Boston

JEWISH MEMORIAL HOSPITAL

The next staff meeting of the Jewish Memorial Hospital will be held in the hospital auditorium, 45 Townsend Street, Roxbury, on Wednesday evening, December 20, 8 30 Dr Richard Ohler will speak on the subject, "Hypertension" A collation will be served

The medical profession is invited to attend

SCHOOL	FIRST TIME		SECOND OR THIRD TIMES		FOURTH OR MORE TIMES		TOTAL		TOTAL APPLICANTS
	PASSED	FAILED	PASSED	FAILED	PASSED	FAILED	PASSED	FAILED	
Middlesex University	12	17	3	21	3	22	18	60	78
Tufts College Medical School*	11						11	0	11
Ghent*			1				1	0	1
Kansas City University of Physicians and Surgeons		2		10		7	0	19	19
College of Physicians and Surgeons (Boston)	1	1		8		7	1	16	17
Mid West College of Medicine (Kansas City)		1	1	5		1	1	7	8
Massachusetts College of Osteopathy†		9		5	2	2	2	16	18
Kirksville College of Osteopathy†		3		2		3	0	8	8
Philadelphia College of Osteopathy†	1	6		1			1	7	8
Edinburgh*	1			1			1	1	2
Lausanne*				2			0	2	2
Prague*		2					0	2	2
Des Moines Still College of Osteopathy†			1				1	0	1
Woman's Medical College of Philadelphia*	1			1			1	1	2
Vienna*	3	2					3	2	5
Northwestern University Medical School*	1						1	0	1
Berlin*	2	1					2	1	3
University of Rochester School of Medicine*	2						2	0	2
Boston University School of Medicine*	1	1					1	1	2
University of Iowa College of Medicine*	1						1	0	1
Freiburg*	1	1					1	1	2
University of Pittsburgh School of Medicine*	1						1	0	1
Georgetown University School of Medicine*	2	1					2	1	3
University of Buffalo School of Medicine*	1						1	0	1
Florence*	1						1	0	1
New York University College of Medicine*	1						1	0	1
Munich*						1	0	1	1
Chicago Medical School	1						1	0	1
Tulane University of Louisiana School of Medicine*	1						1	0	1
University of Michigan Medical School*	2						2	0	2
Harvard Medical School*	7						7	0	7
University of Vermont College of Medicine*		1					0	1	1
Columbia University College of Physicians and Surgeons*	3						3	0	3
McGill University Faculty of Medicine*	2						2	0	2
Loyola University School of Medicine*		1					0	1	1
University of Maryland School of Medicine*		1					0	1	1
Rome*		1					0	2	2
Athens*						1	0	1	1
Missouri College of Medicine and Science†						1	0	1	1
University of California Medical School*						1	0	1	1
Emory University School of Medicine*	1						1	0	1
University of Virginia Department of Medicine*	1						1	0	1
Frankfort*	1						1	0	1
Masaryk*	1						1	0	1
St. Louis College of Physicians and Surgeons						1	0	1	1
	65	51	6	56	5	47	76	154	230

Approved schools
†Osteopathic schools

Approved schools	50	127‡	1	4‡	0	3‡	51	191‡	70
Not approved schools	14	21	4	44	3	39	21	104	125
Osteopathic schools	1	18	1	8	2	5	4	31	35
	65	51	6	56	5	47	76	154	230

‡The exponents represent graduates of European schools

BOSTON DOCTORS
SYMPHONY ORCHESTRA

The Boston Doctors Symphony Orchestra will rehearse under Alexander Theide, former concert master with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra, every

Thursday at 8.30 p.m., in Studio A Station WMBX 6 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr. Julius Loman, Chatham Hall Hotel Brookline (BEA 2430).

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday December 20, from 2 to 4 p. m. Drs. Elliott C. Cutler and Somers will speak on "Jaundice." A clinicopathological conference, conducted by Dr. Elliott C. Cutler will take place from 4 to 5 p.m.

On Thursday, December 21 from 8.30 to 9.30 a.m. there will be at the Peter Bent Brigham Hospital a combined clinic, conducted by Dr. Elliott C. Cutler of the Medical Surgical Orthopedic and Pediatric Services of the Children's Hospital and the Peter Bent Brigham Hospital. Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER M.D., Secretary

MASSACHUSETTS DEPARTMENT OF CIVIL
SERVICE AND REGISTRATION

MEDICAL ADVISER DEPARTMENT OF INDUSTRIAL ACCIDENTS
Director of State Civil Service Ulysses L. Lupien, has today announced that a competitive examination is to be held on January 6 to find eligibles for appointment to position of Medical Adviser Department of Industrial Accidents. The minimum salary is \$4200 a year the maximum \$5100. The duties are as follows to examine medical testimony given by physicians and technicians at trial proceedings to make physical examinations of injured workmen and submit opinions and diagnoses as to liability and causal relation to injury to advise the Industrial Accident Board as to the selection of competent medical-disease referees and impartial physicians to interpret medical problems and terminology for the members of the Board to systematize and supervise the personnel of the medical unit of the department. The appointees be permitted to carry on private practice to such extent as is approved by the Department of Industrial Accidents.

Entrance requirements are as follows applicants must be physicians licensed to practice medicine by the Massachusetts Board of Registration in Medicine and must have been members of the medical or surgical staff of a hospital approved by the American College of Surgeons.

Subjects and weights are as follows training and experience, 2 practical questions, 3 total, 5 Applicants must obtain at least 70 per cent in each subject of the examination in order to become eligible. Physical fitness to be determined by physical examination. The last date for filing applications is Saturday December 13 1939 at noon.

NEW ENGLAND SOCIETY
PHYSICAL MEDICINE

The annual meeting of the New England Society of Physical Medicine will be held on Wednesday evening,

December 20 at the Hotel Kenmore, Boston. An informal dinner will be held in the Empire Room at 6.30.

PROGRAM

Tumor Formation in the Mineral Vegetable and Animal Kingdom (illustrated by slides) Dr. William S. Bambridge. Discussion by Drs. Halsey B. Loder and William D. McFee.

All members of the medical profession are cordially invited to attend.

WILLIAM D. McFEE, M.D., Secretary

AMERICAN ORTHOPSYCHIATRIC
ASSOCIATION

The seventeenth annual meeting of the American Orthopsychiatric Association, an organization for the study and treatment of behavior and its disorders, will be held at the Hotel Statler Boston on February 22, 23 and 24 1940.

NORVILLE C. LAMAR, Secretary

UNITED STATES CIVIL SERVICE
COMMISSION EXAMINATIONS

Junior Medical Officer (rotating internship) \$2000 a Year
Junior Medical Officer (psychiatric resident) \$2000 a Year

The place of employment is to be St. Elizabeths Hospital Department of the Interior Washington, District of Columbia. Applications for these positions must be on file with the United States Civil Service Commission Washington District of Columbia, not later than January 2.

For the position of Junior Medical Officer (rotating internship) applicants must be fourth-year students in a Grade A medical school. For the position of Junior Medical Officer (psychiatric resident) applicants must have successfully completed four years of study in a Grade A medical school subsequent to December 31 1936, and they must have successfully completed an internship of at least one year provided that applications will be accepted from persons now serving an accredited rotating internship.

Full information regarding these examinations may be obtained from the secretary of the United States Civil Service Board of Examiners, at any first-class post office, from the United States Civil Service Commission, Washington, District of Columbia or from the United States Civil Service district office at Boston.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING
MONDAY DECEMBER 18

MONDAY DECEMBER 18

12.15 p.m.-1.15 p.m. Clinicopathological conference. Dr. S. Burr Weisbach. Peter Bent Brigham Hospital amphitheater.
8.15 p.m. New England Heart Association. Peter Bent Brigham Hospital.

TUESDAY DECEMBER 19

10 a.m.-12.30 p.m. Boston Dispensary tumor luncheon.
12 m. South End Medical Club. 11 quarters of the Boston Tumor Society. Avenue 354 Columbia A. case, Boston.
12.15 p.m.-1.15 p.m. X-ray conference. Dr. Merrill C. Newman.
Peter Bent Brigham Hospital amphitheater.

WEDNESDAY DECEMBER 20

12 m. Clinicopathological conference. Children's Hospital amphitheater.
2 p.m.-4 p.m. Joint medical and surgical clinic. Peter Bent Brigham Hospital.
8.15 p.m. Boston Lying-in Hospital.

THURSDAY DECEMBER 21

8 30 a.m.—9 30 a.m. Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital at the Peter Bent Brigham Hospital

FRIDAY DECEMBER 22

*10 a.m.—12 30 p.m. Boston Dispensary tumor clinic

Open to the medical profession

DECEMBER 15—New England Roentgen Ray Society Page 917 issue of December 7

DECEMBER 15—Waltham Hospital Clinicopathological conference. Page 880 issue of November 30

DECEMBER 15—Boston Dispensary Clinical staff meeting Page 916 issue of December 7

DECEMBER 15—United States Marine Hospital Page 918 issue of December 7

DECEMBER 18—New England Heart Association Page 917 issue of December 7

DECEMBER 19—South End Medical Club Page 917 issue of December 7

DECEMBER 20—Boston Lying in Hospital Page 917 issue of December 7

DECEMBER 20—Jewish Memorial Hospital Page 956

DECEMBER 20—New England Society of Physical Medicine. Page 957

DECEMBER 20—Peter Bent Brigham Hospital Joint medical and surgical clinic Page 957

DECEMBER 21—Combined clinic of the medical surgical orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital Page 957

DECEMBER 22—Waltham Medical Club Page 880 issue of November 30

DECEMBER 27—Metropolitan State Hospital Clinicopathological conference Page 880 issue of November 30

DECEMBER 29 and 30—Phi Delta Epsilon Page 918 issue of December 7

JANUARY 6 JUNE 8—11 1940—American Board of Obstetrics and Gynecology Page 160 issue of July 27 and page 798 issue of November 16

JANUARY 11—Pentucket Association of Physicians 8.30 p.m. Hotel Bartlett Haverhill

JANUARY 22—25 1940—American Academy of Orthopaedic Surgeons Hotel Statler Boston

FEBRUARY 11—14—International College of Surgeons Page 759 issue of November 9

FEBRUARY 22 23 and 24—American Orthopsychiatric Association Page 957

MARCH 2 JUNE 8 and 10—American Board of Ophthalmology Page 719 issue of November 2

MARCH 7—9 1940—The New England Hospital Association Hotel Statler Boston

MAY 14 1940—Pharmacopoeial Convention Page 894 issue of May 25

JUNE 7—9 1940—American Board of Obstetrics and Gynecology Page 1019 issue of June 15

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 3 1940—Semi-annual meeting Combined meeting with Essex South Danvers State Hospital Hathorne 7 p.m.

ESSEX SOUTH

JANUARY 3 1940—Head Injuries Dr. John S. Hodgson Danvers State Hospital Hathorne

FEBRUARY 14—Cough Sputum Hemoptysis—How shall they be investigated? Dr. Reece H. Betts Essex Sanatorium Middleton

MARCH 6—Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections Dr. Champ Lyons Lynn Hospital Lynn

APRIL 3—Addison Gilbert Hospital Gloucester

MAY 8—Annual meeting Salem Country Club Peabody

HAMPSHIRE

JANUARY 10 1940

MARCH 13

MAY 8

All meetings are held at 11:30 a.m. at the Cooley Dickinson Hospital Northampton

MIDDLESEX EAST

JANUARY 10 1940

MARCH 20

MAY 15

Meetings are held at 12 15 p.m. at the Unicorn Country Club Stoneham

MIDDLESEX NORTH

JANUARY 31 1940

APRIL 24

JULY 31

OCTOBER 30

NORFOLK SOUTH

JANUARY 4 1940

FEBRUARY 1

MARCH 7

APRIL 4

MAY 2

All meetings with the exception of one which is usually held at Quincy City Hospital are held at the Norfolk County Hospital in So. Braintree, at 12 o'clock noon

PLYMOUTH

JANUARY 18 1940—Brockton Hospital Brockton

MARCH 21—Goddard Hospital Brockton

APRIL 18—State Farm

MAY 16—Lakeville Sanatorium, Lakeville

SUFFOLK

JANUARY 31 1940—Scientific meeting Subject to be announced later

MARCH 27—Scientific meeting Symposium on Ulcerative Colitis and Diarrheas Under the direction of Dr. Chester M. Jones

APRIL 24—Annual meeting in conjunction with the Boston Medical Library Election of officers Program and speakers to be announced later

WORCESTER

JANUARY 10 1940—Worcester City Hospital

FEBRUARY 14—Worcester State Hospital

MARCH 13—Worcester Memorial Hospital

APRIL 10—Worcester Hahnemann Hospital

MAY 8—Worcester Country Club

Each meeting begins with a dinner at 6 30 p.m. and is followed by business and scientific meeting

BOOK REVIEW

Treatment by Diet Clifford J. Barborka Fourth edition, revised 691 pp. Philadelphia, London and Montreal J. B. Lippincott Co., 1939 \$5.00

The amazing advances in the knowledge pertaining to vitamins have focused attention on problems of diet. The unfortunate economic plight of many has furnished an array of bizarre clinical forms of vitamin deficiencies, and extensive opportunities for therapeutic application of this knowledge have thus become available. The author of this book discusses the vitamins in a succinct yet adequate manner, although the interminable flow of facts cannot be covered by any textbook. His castigations of the exploitation of vitamins over the radio and in other ways, which unfortunately at present is beyond medical control, is well founded.

The book discusses dietetics from three aspects: diet in health, the application of diet therapy, and diet in disease. The greater portion of the book is devoted to tables from which can be culled the appropriate diet under various conditions. Throughout the volume a rational physiological approach is emphasized.

In the section on ulcer therapy one notes the omission of any mention of the Meulengracht regime of early and liberal feeding following hematemesis and melena and of the use of the Andresen gelatin mixture for the same purpose. Out of deference to its originator the Sippy diet should have been reproduced as he devised it, the modifications, however, are sound.

Whether intravenous alimentation by means of amino acids will prove feasible is sufficiently debatable to warrant omission. Too much stress is placed on liver as such in the treatment of pernicious anemia, the various extracts have demonstrated their merit and convenience. The reviewer doubts that allergists would place any fever as we know it, in the food allergy group.

Since most medical schools offer insufficient instruction in dietetics, a volume of this type is valuable. Furthermore it will undoubtedly be of use to the practitioner for daily reference.

The New England Journal of Medicine

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VOLUME 221

DECEMBER 21, 1939

NUMBER 25

MEDICAL PROBLEMS OF THE DAY*

ROCK SLESTER, M.D.†

WAUWATOSA, WISCONSIN

FOR many years we have noted with growing concern the gradual development in certain quarters of an entirely artificial sentiment for the introduction into this country of foreign systems of medical care. This has been brought about by well-financed propaganda, skillfully directed by professional promoters and carefully disguised in the name of humanitarianism.

Until eight years ago, when our country followed others into the state of world wide depression, the campaign made little headway and attracted little attention. A period of the greatest prosperity ever known was then followed by unemployment, and a large part of our people who had failed to save for a rainy day found themselves in actual want. Others were forced to curtail and economize. Standards of living never before enjoyed by any people were lowered. As a result, necessities became more difficult to attain and many luxuries became impossible to enjoy.

Conditions have not improved. All this has contributed to a state of mind in which people are ready to seize upon any scheme promising enhanced social security. A people formerly employed and independent have become susceptible to promises of panaceas, with little inclination to consider deliberately the price they will be forced to pay for them. The proponents of these plans either fail to understand or have failed to present the problem of medical care as a part of the whole economic picture.

While we hear much of the ill fed, the ill housed and the ill-clothed, little if anything is said of these problems as they relate to the creation of a medical problem. Physical needs as a contributing cause of illness get scant attention with the spotlight focused on medical needs alone. The cart is put before the horse, and unemployment is almost entirely attributed to illness, rather than much illness to the needs created by unemployment. This attitude is held in the face of mil-

lions in the ranks of the unemployed who are physically well yet unable to find work. Cause and effect are ignored and we are asked to concentrate on effects and ignore causes. The results of haphazard and unscientific surveys of small cross-sections of the population, conducted by inexperienced relief workers, are quoted as fact and are placed for interpretation and analysis in the hands of admitted proponents of schemes of reform. Their conclusions are presented as a new discovery. No consideration is given to the fact that the problem of medical care is as old as the world. No comparisons are made with the problem as it existed in earlier times, and no mention is made of the fact that it goes hand in hand with the question of providing food, shelter, clothing, heat and light.

Whatever criticism may be aimed at the American Medical Association, the fact remains that the medical profession, voluntarily and from a sense of duty is responsible for almost everything of social value in the healing arts today. It seems scarcely necessary to enumerate here the benefits to the people of this country which can be credited to organized medicine alone. In the last half century no science has advanced so rapidly, and no benefits have been brought so promptly and unselfishly to the benefit of the public. We have been so engrossed in our work, however, that we tacitly assumed that public opinion was correctly evaluating these benefits and giving credit where credit was due. This indeed was true until a storm of propaganda was let loose representing the medical profession as backward selfish and indifferent to public needs. Books, news releases, magazine articles, interviews and speeches have appeared with startling regularity, a regularity which leaves little doubt that they are inspired.

The evident purpose of this propaganda has been to give the impression that there are definite critical needs which the medical profession has been derelict in meeting. We have failed to see the farmer blamed for lack of food, the land

*An address presented at the annual meeting of the New Hampshire Medical Society at Manchester, June 9, 1939.
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lord blamed for lack of housing or the manufacturer blamed for lack of clothing. The supplying of these wants is readily admitted to be the responsibility of society. Medical needs, however, by some peculiar line of reasoning are presented as the responsibility of the medical profession, and their existence as due to the stubborn failure of the profession to recognize and meet them. No credit is given to a profession which has given a million dollars a day in free service, and millions more in service rendered at a charge less than its cost. What comparable record have the purveyors of other necessities of life to offer? What other group of workers has so unselfishly admitted and met social emergency? Yet we are threatened with government intervention unless we correct a need coexistent with every other necessity, a need which we did not create, a need which thousands of others have failed to correct.

The threat of a political agency, which has so failed in its effort to bring back prosperity through new philosophies, to take over the problem of medical care is the height of absurdity, and would be tragic in its consequences. The mills of the propagandist grind on, week by week and month by month. Expressive terms appealing to the emotions are used to designate the medically needy, until an entirely unproved condition is accepted as a fact, even by some outstanding members of our own profession.

Charges against a profession above reproach have culminated in an indictment by a grand jury. Defense of the quality of medical service and the disapproval of an experiment which could lead only to a competitive practice of commercial groups, each underbidding the other, have led to charges that the American Medical Association is a monopoly acting in restraint of trade. The profession is accused of being insensitive to the social currents of a changing world. We are pictured as a group dominated by old men, a term stringently reminiscent of that applied to an independent judiciary. A recent magazine article of the so-called liberal type announces that organized medicine is doomed unless it is democratized. We are advertised on the pages of another periodical as money-mad doctors. We are libeled and threatened with a regularity which shows both method and purpose. God help us, for we too have differed with the all-wise, have called attention to their inaccuracies, have disputed their diagnosis and have refused to be stampeded into agreement with un-American and revolutionary doctrines.

Any attempt to appraise or evaluate the problem as a whole must take into consideration the

background and history of the medical profession. Each step in its advance has been a battle against ignorance, suspicion and political and selfish interests. The present situation is not a new one, for the history of the practice of medicine is the history of a continued defense against its enemies. Scientific medicine of today, with all that has been accomplished, has been made possible only by the willing self-sacrifice of medical men. Can we do less today?

Recall, if you will, the opposition faced in developing public-health measures. The wars on smallpox, on typhoid, on malaria and on yellow fever were constantly handicapped by organized opposition and high influence. Gorgas was near failure in Panama because of bureaucratic persecution. At one time nearly every town of any size boasted one or more private medical schools. The present standards of medical education have been made possible only by the courageous work of the Council on Medical Education, yet no body of unselfish workers has been subjected to greater abuse. I am not an oldster, but I recall the days of Lydia Pinkham, electric belts, the traveling advertising quack and the Indian medicine show. I recall the time when the existence of most medical journals depended on the advertising of worthless proprietary preparations and apparatus. I remember the slander suits brought against the officers of the Association because of its campaign against quackery and dishonest advertising, and the alarm felt a quarter of a century ago because of the plague of cult practitioners seeking a short cut to care for the sick. In defense of scientific medicine, we were then, as now, accused of being a high-handed monopoly. I recall the efforts required to develop and perfect our public-health service and our laws relating to license for the practice of medicine. There was determined opposition at every turn.

Is all this the story of a group indifferent to human need? Is this a story of selfishness? Were these benefits for the physician? Or has there been enacted the drama of an idealistic profession fighting to wipe out the diseases which furnish it a livelihood, battling to protect its people against fraud and striving at all times to defend the advancement of science, and honesty in its application?

The National Health Conference, called by the federal Interdepartmental Committee to Coordinate Health and Welfare Activities, was held in Washington in July, 1938. The proceedings were widely publicized. At this meeting a national health program was announced and definite proposals were made. During September the

House of Delegates of the American Medical Association, representing 114,000 American physicians, was called into special session to consider these proposals and to formulate the policies of the Association as it related to them. The results of this conference have been reported to you by your delegates, and have been published in the *Journal of the American Medical Association*. In the consideration of these proposals, the House was motivated by but one thought — if enacted what would each contribute to the prevention of disease, the prolongation of life and the alleviation of suffering, and at what cost would this be accomplished? In other words what price glory? To what would it lead? Were questionable temporary advantages to be lost and offset by later disadvantages? To those plans which would benefit the people we serve we have offered our whole hearted and unselfish support that was our plain duty. It was equally our duty to oppose in every way at our command unsound doctrines which would eventually lower the quality of medical service to the level of that in other countries, where the physician has been made subservient to political control.

Since the meeting of the House of Delegates, the recommendations of the Technical Committee and the Interdepartmental Committee have been considered by three other national bodies of public servants to the sick — dentists, hospital administrators and public health officers. These associations have arrived at conclusions surprisingly uniform with the policy established by the House of Delegates. The first two expressed frank opposition to compulsory health insurance. The American Public Health Association failed to endorse the proposal and thus it implied disapproval.

Our critics have continued a campaign of publicity in order to create the impression that organized medicine has failed to present a program that government agencies have thus been forced to do so and that here at last is the way to the promised land. Let medicine accept it, or be convicted of torquism and forever hold its peace. The action of the House of Delegates in endorsing every constructive element in the program is an answer to these charges. But was this so-called program in any respect new? It contains not a single constructive benefit which has not been advocated year after year by the medical profession. The main difference is that the new program specifies the number of million dollars required. That part of it concerned with the administration of compulsory health insurance has been included in the programs of all socialistic and communistic types of government.

This is an appropriate point at which to com-

ment on the so-called National Health Program, and the report made on it by the Technical Committee. Because I represent the practice of medicine, and would be accused of bias, I shall refrain from making any personal comment.

Since this was a National Health Conference, let us see what one of America's leading health authorities had to say on the subject. I quote from an address made before the New Jersey Health and Sanitary Association last November by Dr. Haven Emerson,* professor of public-health practice at Columbia University. Let us remember that this is the appraisal of a man who has given his life to public health work and who is not now, and never has been, engaged in the practice of clinical medicine.

We may ignore the errors of fact, of social theory and of methods employed by the present federal administration to promote acceptance of its proposals. However it is obvious that the evidence on which the extravagantly phrased descriptions of the existing state of health and medical services in the United States appear to have been based are inadequate to answer the questions at issue or to carry conviction to any but a credulous lay public.

What has been published as a National Health Survey was nothing of the kind and what was publicized as a National Health Conference was not a conference at all but a sounding board before which a hand-picked and in the main a preconvinced group of invited guests listened to the report of a technical committee, with the doubtful privilege of extemporaneous comments but no opportunity for collective consideration or adoption of the slightest change in the ready-made proposals which they were assembled to endorse. To describe the present state of the public health services of our country as grossly inadequate is a mischievous untruth and expresses an emotional unbalance in the thoughts and experience of the technical committee members unworthy of persons trusted with national statesmanship.

We are now in fact the possessors of better general health, are less afflicted with preventable disease, are more secure in the survival of our offspring to maturity and have an average expectancy of life greater than that of any population group in the history of man, comparable in size, variety of races and distribution in age, occupation and economic and climatic conditions. We are today at the very zenith of a march of progress toward national health. Never before in this or any other continent have any 130,000,000 people recorded such low death rates as will be reported in the United States for the year 1938 for all causes, for tuberculosis, typhoid, diphtheria and infant mortality. Not in our time has maternal mortality been so low or the death rate from pneumonia. Nothing new has been proposed, only a larger grant of money aid to the states from which the money was originally taken to the detriment of their own local programs.

That a high quality of care has been given to the sick poor in the past is generally admitted and is attested by adequate statistical proof of the reduction in

Emerson, H. Sign of the times in public health. I. A. M. A. 112: 27
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morbidity and mortality to their present low levels among such persons

Some people will always need medical attention, but the reasons for this are not largely, if at all, the inability of these sick to pay for the cost of necessary treatment but chiefly result from ignorance, superstition and misinformation growing out of religious beliefs and faith in the promotion of advertised medications. That anything like one third of the sick now lack medical care or that an even larger proportion of the population are hindered from gainful employment by preventable and remediable but uncared for disease, as the peroration of the technical committee would try to persuade us with statistics and emotional publicity, is just so far from the truth that it will be forgotten by the public and by the physicians of this country who know it is not so.

Obviously the purpose of the Wagner Bill, as introduced in Congress on February 28, 1939, is to gain fulfillment of the so-called National Health Program although the measure is in many of its recommendations exceedingly vague. It authorizes the appropriation of vast sums of money before the need for them has been shown by any dependable study. The advisory councils to be set up are vague as to their membership, their duties and their responsibilities. Open to criticism above all else is the extreme vagueness of the bill, in the light of the vast sums of money to be expended, and the wide powers to be conferred on some federal officers in the control of spending, and particularly in the decision as to which of the individual states shall benefit by the expenditures.

The introduction of this bill was the culmination of several years of preparatory propaganda intended to convince the uninformed that there had been a breakdown in medicine as in agriculture, industry, railroads, manufacturing and building. This is not true. In fact, medicine is almost the only major line of endeavor which has not failed, on the contrary, it has improved the quality of its service as well as its distribution during the depression years. This is shown by the lowest mortality and morbidity rates, those for 1938, that any country has shown in the history of the world. Such needs as exist are only those co-existent with the needs of the necessities of life, and they have been met by American medicine as no others have been.

It is indeed difficult for the medically trained mind to agree with Senator Wagner's diagnosis or prescription. It is hard to conceive that the mere spending of millions of dollars is going to prove any more efficacious than it has in other ills receiving the same treatment for the past six years.

As I go about the country, one question more than any other is asked by both the laity and the members of our profession, and this question shows the effect of continued propaganda and misinformation. It is this: Why does not the Ameri-

can Medical Association do something or bring out a plan? When the members of our own profession ask this question, is it any wonder that lay people do? Let us try to answer it.

In the first place, the delivery of medical services is only part of a whole. Let us ask why the farmer does not do something about the food question, why the clothier does not do something about the clothing question, why the landlord does not do something about the housing question.

Second, with the United States Public Health Service and the Metropolitan Life Insurance Company both reporting within the last few months the lowest mortality and lowest morbidity in the history of this or any other country, is there any new or pressing or critical problem, requiring a revolutionary overthrow of all that has been so patiently built up through all the years? Granting that there has always been and always will be room for improvement, is the situation so urgent that we must be stampeded into giving up an orderly, rational procedure, which has brought American medicine and American health to the highest point in history, for European panaceas that have all but wrecked medicine in these countries? In view of these reports, let no one tell you that one third of the people of this country are without adequate medical care.

Third, there are today more than three hundred so-called plans being tested in various parts of the country. Can any thinking person believe that one plan would fit the needs of all communities? To do so is just as absurd as to expect a standardized pair of shoes to fill the needs of all who wear shoes. Plans must be fitted to individual conditions, just as treatment is fitted to the individual patient. A plan that fits an Eastern industrial center would not be suited to a Western community. A plan adequate to fill the needs of a Northern agricultural section would be worthless in a Southern Negro settlement. So let us stop talking about a plan.

Fourth, to expect the American Medical Association to "do something about it" is mere wishful thinking and evasion of responsibility. Who and what is the American Medical Association? You are the American Medical Association, of course, and if you who live in New Hampshire ask the American Medical Association to do the job for you, you are merely asking your neighbors to take on your responsibilities. Do the medical men of Alabama, Texas, Michigan or Ohio know your problems as you know them? Do you want them to prescribe for your patients without seeing them?

What you often thoughtlessly refer to as the American Medical Association is a building in

Chicago—a clearing house where paid employees make available to you any and all important information, a helpful unit jointly established and maintained by all state and county societies. It is your servant, not your master, and no employee, no board, no officer may establish policies for you to follow. They can only carry out the policies established by the House of Delegates, a truly democratic body, in which you have the same proportionate voice as any component state society.

I am here today not to advocate a policy of my own but to give my support to the policies you have laid down for me to follow. The answer to the problem of improvement in the distribution of medical care in any community is in the hands of its own physicians, and God grant that it always remain there.

The doctor as we know him plays no part in the scheme of machine medicine. Socialized medicine is medicine by rule. Patient and doctor alike are mechanized on an efficiency-production basis. The art of medicine is destroyed by political and business administration; human relations are lost with the introduction of a third party between the doctor and his patient. The patient becomes a mere case, to be recorded on the insurance report at the end of a busy day, and the doctor, rule book in hand thumbs the pages to see whether he has exceeded his authority. Those sponsoring this system of medicine have no understanding of what we mean when we refer to personal relations or insist on individualistic practice. They admit medicine to be a service, but regard it as something that can be measured, dispensed by chain-belt methods and recorded by bookkeeping.

This cannot be, for medicine must be a personalized service. Medical knowledge is a science, but its application to the sick person is an art. We do not treat textbook pictures, so treatment can not be standardized. X-ray films and laboratory procedures are but aids, and the physician cannot tabulate their results on an adding machine and by the turn of a handle get the sum of a diagnosis. Identical treatment is as rare as identical twins. The potency of a drug can be standardized but who can standardize its administration to different patients? We are each different individuals, with different reactions to disease, with different reactions to treatment and with different reactions to those circumstances in life which influence our mental and emotional status. Just as we have different fingerprints so do we have different heart capacities under strain. We are of different ages, sexes, builds, weights, resistances, inheritances and temperaments, and one can only

be an individual in his illness, demanding and yearning for individual treatment and individual care. So it is that medicine does not lend itself in the art of its application to the mass-production methods of a modern industrialized and socialized society. Delivery of medical care can never be the furnishing of a packaged product.

I am proud of medical men who are caring for the great masses of our people. I am proud of the record they have made. I am proud of men who are traveling lonely country roads at night, men who are bringing babies into the world at daybreak, men who are taking the responsibility of human life in the operating room, men who are saving sick children, men who are easing the pain of the aged, men who are friends, counselors and fathers to their people. These are the men who go to make up the American Medical Association.

Faithfully attended, the meetings of this association are given over to a serious study for improving service to the sick. Hours and wages have never been subjects for discussion. Its resources are spent on educational endeavors, in order that its members may better serve. Its publications are devoted to the science of medicine, in order that all that is new may be brought to the bedside of the sick, even in the most remote districts. I challenge anyone to find in the pages of these publications anything that reflects in any way a selfish interest.

The discoveries of the medical profession are given freely and promptly to humanity without individual profit. Its services are given within the means of the receiver to pay. Its charities are unequalled in the history of the world. Its advancement in self-improvement has never been rivaled. Expectancy of life has been doubled, and the world has been made a better, safer and happier place in which to live a life lengthened through its efforts. Fraud and quackery have been exposed and legislation protective to the people has been enacted. Education has been advanced and hospital standards elevated. The people have been taught how to avoid illness, and research has been encouraged and financed. The highest standard of ethics of any profession or trade the world has ever known has been required of the members of the American Medical Association. This is the organization of which I am proud, yet this is the organization which has been accused of being backward, conservative, selfish and indifferent to human needs.

American medicine has never stood still. We are deeply conscious of improvements to be made in the distribution of medical care. We believe that no plan can be successful without the whole

hearted co-operation of the medical profession, and that the Government, if sincere, will recognize that fact. We have recognized one, and only one, great responsibility—that to the people of our country. We have offered our hearty co-operation in perfecting our services to them. We will, however, not be a party to any plan which lowers the quality of medical service to even the poorest family. Maintaining our constant advance in the science of medicine, we are dedicated to a distribution of the highest type of medical service possible to the people at a price they can afford to pay. The care of the sick must not be given over to commercial groups in open competitive bidding, each offering a little more for a little less. It must not be dominated by political control. In the development of any plan, it is our plain duty to the American people to see that the

structure of medicine is not wrecked, for the future health and happiness of our people depend on its constructive advance. It must not be destroyed.

In peace or in war, the medical profession has never failed the people of this country. It will not fail them now. Their needs are our needs, and they will be met as they have always been met by those who through daily contact with the sick know these needs better than any other. Our record is an open book, and we invite full comparison of our unselfish and efficient public service with that of any other agency.

American medicine stands united, proud of its record, loyal to its ideals and dedicated to those policies and principles which are necessary to ensure to the people of this great country the highest standards of medical service.

FURTHER EXPERIENCES WITH POTASSIUM SULFOCYANATE THERAPY IN HYPERTENSION*

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BOSTON

IT IS a commonly accepted fact that many hypertensive patients carry a pressure which is dangerous, and that it is desirable to reduce this excessive circulatory load lest cardiac congestive failure, cerebral accident or other complications take place. The physician faced with such a problem may have recourse to several therapeutic maneuvers. He may advise the patient to take adequate rest, avoid mental and physical strain, bring his weight to a more ideal level, eat simple foods in small amounts, limit his fluid intake to reasonable levels and avoid excesses of any nature. If he adds to this a mild sedative, he will have given his patient what forms the backbone of our present-day therapy. To be sure, certain symptoms and signs demand specific drug therapy, but, by and large, drugs have been of comparatively little value.

Too frequently the above treatment leaves the patient with intravascular pressures that are still excessive, and the physician is left with a choice of offering his patient one of the various surgical operations or some of the recent depressor substances derived from kidney extracts. While we admit that there are some undoubted surgical successes, we believe that proved cases are relatively

few and that the whole problem of surgical therapy is still in a highly experimental state. What has just been said of surgery is even truer of the recently developed renal depressor extracts, which have yet to be properly evaluated.

What resource is there, then, for the physician faced with the problem of the patient who still carries an excessive intravascular load in spite of carrying out carefully the usual treatment outlined above?

About ten years ago, treatment of hypertension by the cyanates, originally initiated by Pauli¹ in 1903, and revived largely through the efforts of Westphal,² Nichols³ and others, bade fair to become quite popular in this country. Wider experience,⁴⁻⁹ however, indicated that the drug while very effective in reducing pressures in certain cases was wholly ineffective in others. Furthermore, there were far too many reports of such serious toxic effects as angina pectoris, cerebral thromboses and serious psychoses. One of the most damaging reports was that made by one of us (J.P.O'H.) in collaboration with others.¹⁰ As a result of these unsatisfactory and often highly disturbing effects, this form of therapy rapidly lost its popularity.

In 1936, Barker¹¹ published a highly illuminating paper in which he disclosed the reason for many of the bad effects of cyanate therapy. He found that different individuals cleared themselves of the drug at very different rates. A given dose

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use where renal clearance was rapid, therefore, to be wholly ineffective, whereas the same in a case where clearance was slow might have an excellent depressor effect. Through a marked heaping up of the drug in the stream the severe and highly toxic effects readily explained. Barker showed that by dualizing the dosage through control of the cyanate level a satisfactory depressor effect be obtained and most of the disturbing toxic be avoided.

Interest in the drug was revived by this and we decided to try it again with extra caution and under rigidly controlled conditions. The preliminary results, published by Masbridge and O'Hare,¹² confirmed the work and made us desirous of trying this therapy in a much larger group of patients. The report records our experiences during the year with 75 patients.

In this series, all but 7 cases were those of unclassified vascular hypertension. Previous experience with the toxic effects of this drug taught us to restrict its use to patients who had had no angina pectoris, congestive heart failure, or accident or significant renal failure. The ones, which were deliberately chosen in spite of previous exceptional histories, will be discussed in this paper.

Throughout the entire period of observation, all patients were instructed to follow our usual routine therapy of adequate rest, moderate exercise, control and avoidance of strains and exertion of all kinds. No drugs were to be voluntarily taken, with the exception of a sedative necessary for sleep.

METHOD OF TREATMENT

Out of 4 patients had been observed for at least three months before cyanate therapy was started, and 33 had been followed for more than a year. During the control period some form of therapy, usually 15 or 30 mg of phenobarbital tablets a day, was given. Potassium sulfocyanate was administered as the potassium salt in a 5 per cent solution of syrup of ipecac. Accuracy of dosage was attempted by having the patient use a small measuring glass at 4 cc so that a unit dose of 0.2 gm might be readily available and accurate. Most patients started on three daily doses of 0.2 gm for 14 days. The dosage was then dropped to twice or the remainder of a week. At the end of the time the patients were examined. Specific therapy was made as to toxic symptoms and the blood pressure was taken. A sample of blood was taken for cyanate concentration. If there were no toxic symptoms and no drop in pressure, ther-

apy was continued with two doses daily. Thereafter, dosage was regulated by the blood-cyanate and blood-pressure levels. Patients were seen approximately once a week during the first six or eight weeks of therapy or until the blood pressure had dropped to an optimum level and the blood cyanate remained at a fairly constant concentration without toxic symptoms. When this stage was reached the time interval between visits was increased to two or three weeks, and occasionally to as long as a month.

On such a program it was found that, in order to obtain a therapeutic response at a satisfactory cyanate level, some patients required only 0.2 gm three times a week while others required as much as 1 gm a day. This emphasizes the point that in order adequately to treat patients with cyanate the dose of the drug must be strictly individualized. It also explains why the routine method of giving the same dose to all patients resulted in the past either in failure to obtain an adequate fall in blood pressure or in a high percentage of toxic manifestations.

RESULTS OF TREATMENT

In the evaluation of any form of therapy for hypertension one must take into serious account the marked variations that normally occur in the hypertensive state, and particularly the psychological effect of any new form of therapy. If one desires the truth about the effect of a given treatment, he should not recommend it highly to the patient, but rather adopt a non-committal or even pessimistic attitude toward it. In this series we have taken these factors into consideration so far as is possible in assaying the value of our treatment.

For simplification of presentation and for fair comparison, all blood pressure readings recorded in each case during the control period as well as all readings while under therapy were averaged. The average reading during the period of treatment was subtracted from the average control reading. Table I summarizes the pressure-reduc-

TABLE I Blood Pressure Reducing Effects of Cyanate Therapy

PRESSURE DROP OF SYSTOLIC EXERCISE		PRESSURE DROP OF SYSTOLIC PER CENT	
MM HG	%	MM HG	%
30	85	10	62
40	63	25	41
45	42	30 or more	16
50	36		
55	19		
60 or more	11		

ing effects thus obtained. A less conservative interpretation of our figures based on maximum rather than average drops discloses still more striking effects. In 3 cases the systolic pressure fell

over 100 mm and the diastolic more than 35 mm. Eight patients had an average lowering of systolic pressure of more than 60 mm, sustained for periods of three to fifteen months. The greatest average fall that was observed was 82 systolic, 34 diastolic, for five months, the next 71 systolic, 35 diastolic, for nine months.

In addition to the definite hypotensive effects noted above, significant relief from symptoms occurred in many patients. The most noteworthy effects were the banishing of the typical severe headache in 18 of 20 patients, a general sedative effect, relief from insomnia and decrease in palpitation experienced by many. Other symptoms such as dizziness and tinnitus were not relieved.

Unfortunately the results noted above do not tell the whole story. With this treatment, we have had failures and disturbing reactions. Nine of our cases were regarded as failures since no significant lowering of pressure was obtained. Examinations of the records for possible causes of failure disclosed only the following facts. Three patients were young and had very high diastolic pressures (± 140). Two were elderly persons with marked arteriosclerosis. Three had to have treatment discontinued because of hallucinations or a severe dermatitis. One patient was simply not adequately treated, the blood cyanate never getting above 6 mg per 100 cc, whereas the optimum level is 7 to 12 mg per 100 cc.

Untoward symptoms or effects were experienced in 29 cases. In the less serious group of 23 cases, the toxic symptoms consisted of weakness, nausea, purpura, mild dermatitis and decreased libido. In 6 cases the complications were of a major order and consisted of such serious difficulties as exfoliative dermatitis, cardiac congestive failure, angina pectoris, cerebral thrombosis and psychoses.

Discussion of some of these difficulties seems pertinent in order to call attention to the necessity for caution in the use of this form of therapy. One of the most frequent manifestations of cyanate toxicity is a sensation of weakness and fatigue, variously described as "lack of pep," "no ambition" and "a lazy feeling." Twelve patients complained of this symptom. Usually it was slight or moderate in degree and did not interfere with treatment. In some cases it occurred early and disappeared after the patient had been treated for a few weeks. In only 2 cases was it serious enough to necessitate stopping therapy, here the degree of weakness was extreme and was associated with a high concentration of cyanate in the blood, 14 mg per 100 cc in one case, and 17 mg in the other. Nausea occurred in only 1 case.

A possible explanation for this great weakness

is offered in some experiments performed by Friend and one of us (RWR)¹³. Through use of the Warburg apparatus it was disclosed that in liver tissue exposed to hypertensive serum containing added amounts of potassium sulfocyanate the rate of oxygen consumption fell as the cyanate concentration increased. It was possible to decrease the metabolism of liver as much as 40 per cent with a concentration of 20 mg of cyanate. Since it is known that cyanate diffuses equally into all extracellular fluids, it was thought that a continuous moderate reduction in the metabolism of all tissues of the body might well be the explanation for the weakness of which these patients complain.

Four types of skin rashes were noted in 8 cases. The most frequent type consisted of reddish macules and small erythematous patches, very similar to petechiae. These occurred most frequently on the volar surfaces of the forearms and over the extensor surfaces of the legs, and were usually accompanied by pruritus. The second type was maculopapular and occasionally pustular, involving the face and the upper portion of the chest and back. It was difficult, at times impossible, to differentiate this type of lesion and a seborrheic dermatitis. Occurring only during the time of treatment and disappearing slowly when the cyanate was withdrawn, it forced us to the conclusion that it must be due to the drug. It is interesting to note that patients with either type of drug eruption behaved in one of two ways. Some were repeatedly sensitive to small doses of the drug, while others developed no rash until the blood cyanate had reached a high level (12 to 17 mg per 100 cc). A third type of lesion, purpura, was noted in 3 cases. Without obvious trauma, ecchymoses 2 to 3 cm in diameter appeared in various parts of the body. As pointed out previously,¹² patients taking cyanate tend to bleed easily from the wound of a venipuncture and from the nose, uterus and so forth, and the purpura may be merely part of this tendency. Unfortunately we did not study the number of blood platelets in these cases.

While the three types of eruption described were quite obvious, they were not bothersome. In 1 case, however, there occurred an extremely disturbing dermatitis exfoliativa involving the entire body, even including the mucosa of the mouth and pharynx. This appeared at a blood-cyanate level of 14 mg per 100 cc. A month passed after the drug was stopped before the lesions entirely healed. It is of interest to note in passing that a pre-existing dermatitis may flare up under therapy. This happened in 2 cases in which there was also a typical cyanate rash.

Two male patients complained of a decrease in libido while receiving cyanate. A normal libido returned when the drug was stopped.

One of the traditional arguments against lowering the blood pressure in hypertensive patients is that they need a certain head of pressure in order to supply the tissues adequately with blood. We have always been apprehensive that we might lower the blood pressure to a point where a thrombosis in a coronary or cerebral artery would occur. To date, no case has developed a myocardial infarction. We have however noted the onset of angina pectoris, associated with a marked drop in blood pressure, in an elderly patient with moderate arteriosclerosis. This occurred when the blood pressure had dropped from 250 systolic, 120 diastolic to 160 systolic, 90 diastolic. The patient for the first time had typical symptoms of angina pectoris, occurring several times a day on exertion. The pain was relieved by rest, the attacks disappeared when the cyanate was stopped and the blood pressure was allowed to return to above 200 systolic. This experience has taught us that too great a reduction in blood pressure, especially in elderly arteriosclerotic patients, is not a wise procedure. A less dramatic but more optimum drop in pressure, from 250 to 200 systolic, would probably have been beneficial to the patient without this serious and annoying complication. We¹² have previously reported a similar case.

In spite of these two experiences, and because Barker¹⁴ had found an increased coronary flow in normal dogs after the administration of cyanate, we selected a willing patient with marked angina and a very high blood pressure (270 systolic, 128 diastolic) in order to see whether lowering the pressure would decrease the angina. The pressure was lowered approximately 70 mm. systolic and 35 mm. diastolic, and the patient had markedly fewer attacks for eleven months under treatment. Unfortunately these results are not so clear-cut as would appear, since the patient lost 20 pounds during the experiment and ate much smaller meals. This last may have accounted for the absence of his customary postprandial attacks. It is of significance, however, that with a much lower blood pressure he had fewer rather than more attacks of angina.

While we may reasonably claim that we decreased the angina in this case, we unfortunately may have caused another circulatory difficulty by lowering the pressure to such a degree. After eleven months he had a cerebral thrombosis with complete hemiplegia. It is difficult to say whether the thrombosis was the result of the cyanate therapy. A blood pressure of 220 systolic, 120 diastolic, immediately after the cerebral accident

made it difficult to determine this point. This is the only case of its kind that we observed during this study. It is interesting to speculate why the thrombosis did not occur in the coronary arteries instead of in the cerebral vessels.

In only 1 case have we noted myocardial failure during cyanate therapy. This occurred in a forty-eight year-old, hypertensive patient who two years previously had had a period of mild heart failure. On bed rest and digitalis, compensation had returned. From that time on in spite of moderate activity, she had had absolutely no sign of heart failure, although she continued to take a maintenance dose of 0.2 gm. of digitalis. The heart was moderately enlarged and the average control blood pressure was 240 systolic, 140 diastolic. In spite of this story of previous congestive failure and because the blood pressure was very high we gave cyanate in addition to digitalis, in order to determine whether the patient would be better off with a lighter arterial load. During the seventh week of therapy with the blood pressure at 150 systolic, 110 diastolic, she began to have attacks of nocturnal dyspnea and rales at both bases appeared. The cyanate was stopped and the patient was treated with rest, digitalis and ammonium chloride. The heart compensated in about two weeks. Within ten weeks of the time of stopping the cyanate the blood pressure had returned to 210 systolic, 120 diastolic. From then on there was no evidence of myocardial weakness. One year later the patient suffered a cerebral hemorrhage, was admitted to the hospital and died in forty-eight hours. The blood pressure on the last admission was 250 systolic, 130 diastolic. This case confirmed our previous impression that it was extremely dangerous to lower the blood pressure with cyanate in cases where there had previously been congestive heart failure.

Much more disturbing to us were the 3 cases in which the patients developed transient periods of hallucinations while taking cyanate. One of the patients was an elderly woman who had previously had a cerebral accident and whose blood pressure before treatment was very high—275 systolic, 150 diastolic. Within one week of starting cyanate, hallucinations appeared at a blood cyanate level of 10 mg. per 100 cc. Although the patient was oriented as to time and place she had hallucinations and ideas of persecution. This lasted for forty-eight hours and disappeared when the drug was discontinued. This patient never again received cyanate. Three months later she had a second cerebral accident and died in another hospital.

The second patient, who was a very high strung, Spanish woman of sixty-four, had a blood pres-

sure frequently ranging as high as 300 systolic, 170 diastolic. After a month of treatment the blood-cyanate concentration was 14 mg per 100 cc. At this time she had hallucinations lasting for thirty-six hours. These disappeared with the prompt discontinuance of the drug. As neither of these patients experienced more than a moderate reduction of pressure, it seems logical to attribute the hallucinations to the toxic reaction of the drug rather than to a suboptimal lowering of the blood pressure.

The third patient, a woman of sixty-three, had a much more serious type of reaction to the drug. She had also had a previous cerebral accident. The blood pressure ranged around 250 systolic, 140 diastolic. With a urea clearance of only 52 per cent of normal, she rapidly built up her blood-cyanate level to a toxic concentration. During the third week of visits to the clinic, the blood

The average control blood pressure on each patient was very high. Each patient had marked evidence of arteriosclerosis in the fundi and at least moderate changes in the peripheral arteries. Kidney function was normal in all but 1 case—in which the blood cyanate was increased quickly to toxic levels and the patient developed a serious psychosis. Perhaps the most significant point is that 4 of these 6 cases should have been excluded by our rule to treat only patients with an uncomplicated vascular hypertension. We knew that 1 patient had had angina pectoris, 1, an episode of congestive heart failure, and 2, cerebral accidents.

The 2 patients who developed mild hallucinations had a reaction to amounts of the drug within the range of that of those having no untoward reaction. The patient who developed the serious psychosis had a cyanate intoxication due to an abnormally high concentration of the drug in the

TABLE 2 Significant Data in Cases with Severe Complications

CASE NO.	AGE	AVERAGE CONTROL BLOOD PRESSURE	BLOOD CYANATE LEVEL	RETINAL ARTERIO-SCLEROSIS	PERIPHERAL ARTERIO-SCLEROSIS	CARDIAC ENLARGEMENT	RENAL FUNCTION	AVERAGE DROP IN BLOOD PRESSURE	PREVIOUS COMPLICATIONS
	yr	mm	mg per 100 cc					mm	
1	55	250/150	10	++	++	++	Normal	14/6	Cerebral accident
2	65	260/120	6-8	+++	++	+++	Normal	68/24	None
3	57	260/140	25	+++	++	+++	Slight decrease	46/14	Cerebral accident
4	63	270/128	7-11	+++	++	+++	Normal	71/35	Angina
5	64	270/145	14	+++	++	+++	Normal	35/14	None
6	48	250/150	7-12	+++	++	+++	Normal	62/29	Heart failure

pressure had fallen from 260 systolic, 140 diastolic, to 230 systolic, 110 diastolic. The patient had been having some slight difficulty in articulation, but this was interpreted as being secondary to the previous cerebral accident. The next day, when the blood cyanate was found to be 22 mg per 100 cc, a far different interpretation was placed on her speech defect and word was sent to her to stop the drug immediately. For some reason she failed to heed this advice and continued to take the drug during the fourth week. At the end of this time the blood pressure was 200 systolic, 110 diastolic, and the blood cyanate 25 mg per 100 cc. She became mentally confused and had motor aphasia, hallucinations and paranoid delusions. Her memory and orientation were poor. She was admitted at once into the hospital and was given fairly large amounts of fluid and salt in an attempt to help her excrete the retained cyanate. In spite of this she eliminated the drug very slowly, taking two and a half weeks to lower her blood cyanate from 24 to 15 mg per 100 cc. At this level she became mentally normal.

The records of these 6 patients who had severe complications during cyanate therapy were studied in an effort to find the reason for them. The significant data are given in Table 2.

The following facts are to be especially noted. Five patients were over fifty-five years of age.

blood. If we had been alert to the situation this complication would probably not have occurred.

The development of angina, cerebral thrombosis and heart failure in the other patients appeared to be due to an excessive drop in blood pressure averaging over 60 mm systolic, 25 mm diastolic, in each case. While younger patients without complications had been able to tolerate even greater falls in pressure, levels were reached in these older and complicated cases of hypertension which brought the local circulation below its minimum effective level.

It is obvious then that some of the complications were due to definite reactions to the drug, while others were associated with excessive drops in blood pressure. It is clear also that most of the severe complications occurred in patients who were exceptions to our previous decision to limit patients to those with uncomplicated vascular hypertension.

DISCUSSION

It seems clear from Table 1 that potassium sulfocyanate administered according to our plan has the power to depress blood pressure in a fairly large proportion of cases of uncomplicated vascular hypertension.

Just what the mechanism is that brings about such effects is still quite uncertain. Barker¹¹ has

tested that there may be a decreased viscosity of the blood—an inference drawn from the lowered blood protein and especially the nitrogen content of the blood. Studies made by peripheral blood flow in these patients so have indicated no effect on the peripheral arteries or arterioles. The most significant data far obtained are those drawn from the experiments with the Warburg apparatus referred to previously. These clearly showed that blood containing cyanate in equivalent amounts to some of the highest levels in man caused a depression in the rate of consumption of liver cells. If we can assume that a similar depression takes place in other tissues we have an adequate explanation for many of the effects we have observed from this drug. The present beliefs concerning the use of sulfocyanate in the treatment of patients with hypertension may be summarized as follows:

Patients should not be over sixty years of age, should not have severe arteriosclerosis or arteriolosclerosis, and should have uncomplicated vascular hypertension, that is, they should not have significant renal disease or have had congestive heart failure, angina pectoris, a cerebral accident or any other disturbance.

Patients should be closely watched for several days after the beginning of treatment. Such observation should take the form of weekly determinations of blood pressure and blood cyanate, examination of the skin for fresh eruptions and inquiry about toxic manifestations. Even the optimum dosage has been determined; the patient must be in contact with the physician, and should be seen at least once a month while taking the drug. Anemia, cabbage goiter and profound leukopenia in blood cholesterol may develop in the long run.

Blood-cyanate concentration should be maintained at the lowest possible level consistent with a therapeutic result. Great care should be taken in using cyanate concentrations above a level of 12 to 14 mg. per 100 cc. since experience shows that higher concentrations may be dangerous. A level of 7 to 12 mg. per 100 cc. appears to be an optimum one.

If a patient fails to respond at blood levels of 4 mg. per 100 cc., maintained for two to three weeks, the treatment should be regarded as ineffective and be stopped. The development of any symptoms or complications other than mild rash or a slight rash calls for prompt cessation.

It is well to stop therapy automatically for one or two weeks every two or three months.

An optimum rather than a maximum drop in pressure should be sought, especially in older patients.

We do not believe that cyanate therapy is the ideal therapy for hypertension, but we do believe that under the conditions here prescribed it adds to the therapeutic armamentarium another effective weapon, which may serve until a better mode of treatment has been devised.

SUMMARY

Seventy-five patients with hypertension were treated with potassium sulfocyanate given by mouth. All were ambulatory. All were followed closely with blood-cyanate studies. Maximum drops in blood pressure of over 100 mm. systolic and 35 mm. diastolic were observed in 3 cases. Average drops of 40 mm. systolic and 20 mm. diastolic occurred in 63 per cent of the patients. Symptomatic effects of the drug were noted chiefly in the relief of hypertensive headaches in 18 out of 20 cases. Toxic symptoms occurred in 29 cases, or 38 per cent. The less serious toxic complications, accounting for 23 of these 29 cases, consisted of nausea, weakness, dermatitis, purpura and a decrease in libido. Serious complications consisting of dermatitis exfoliativa, congestive heart failure, cerebral thrombosis, angina pectoris and psychoses occurred in 6 cases.

From our experience with sulfocyanate therapy, we have concluded that this form of treatment of uncomplicated vascular hypertension in patients under sixty years of age, when carefully controlled has decided value.

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BILIARY SURGERY IN THE AGED*

A Study of 100 Consecutive Cases

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A STRIKING result of the progress of civilization in the past century has been the increase in the average span of life. A baby born in the United States in 1850 had a life expectancy of about forty years. A baby born today can look forward to approximately sixty years of life (Fig 1).^{1, 2} At the same time there has been a decrease

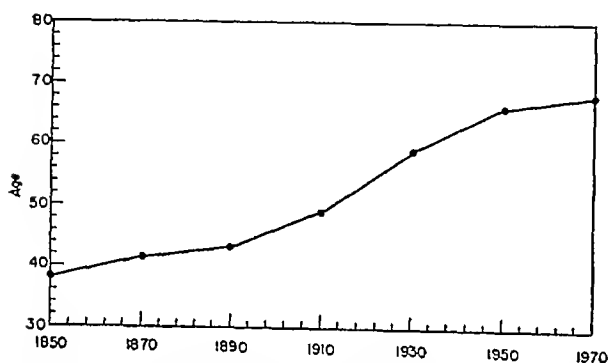


FIGURE 1 The Increase in the Expectation of Life at Birth Massachusetts 1850-1930 and estimated future trend

in the birth rate, and these two factors have operated to produce a tremendous shift in the age composition of the population. Today persons over sixty-five constitute 64 per cent, and in 1980, other things being equal, they will constitute 14.4 per cent. In other words, about 8,400,000 of our present population of 132,000,000 are sixty-five or over, forty years hence they will constitute 22,000,000 of a population of 153,000,000 (Fig 2).¹

It is apparent, therefore, that the medical profession is soon to be confronted with a considerably larger number of aged individuals who, as Brooks³ says, may not tolerate summary dismissal as "too old for surgery." In view of this, certain aspects of surgery of the aged seemed worthy of review.

The surgical treatment of non-malignant disease of the biliary tract was selected for this study because it involves a small number of well-standardized procedures which can be statistically analyzed with reasonable accuracy, and because the incidence of biliary disease increases with age. The latter fact has been well established by the clinical researches of Deaver and Bortz,⁴ Mentzer,⁵ Graham et al.,⁶ Crump⁷ and others. It is illus-

trated in Figure 3, which is based on Crump's exhaustive study of the biliary system in 1000 consecutive routine necropsies at the *Pathologischen Anatomischen Institut des Krankenhauses* in Vienna.

One hundred consecutive cases of biliary surgery on patients over sixty-five years of age at the Peter Bent Brigham Hospital were selected for the present study. The series included 31 men and 69 women. The average age was sixty-nine. Eighty-seven patients were well on discharge and 13 died in the hospital. Thirty-six—12 men and 24 women—were treated as private patients. Of these only 1, a sixty-seven-year-old man with syphilitic heart disease, aneurysm, chronic nephritis, cholangitis and acute cholecystitis, failed to survive operation. The ward patients, therefore, were considerably poorer risks than were those in the private group. This fact must be attributed to inferior economic status and delayed hospitalization, since the bulk of the surgery on these ward patients was done by senior surgeons.

Eight of the 12 ward deaths occurred among 19 men, while only 4 of 45 women succumbed. In 7 of these 8 fatal cases among the men surgery was imperative, 5 patients had acute cholecystitis, and only 1 survived. If the 29 cases in which surgery was imperative be excluded, 3 deaths occurred among 71 patients, a mortality rate of only 4 per cent.

The effect of this factor is also seen in Table 1, in which the series is divided into three

TABLE 1 Mortality in Relation to Principal Diagnosis

DIAGNOSIS	MORTALITY RATES	
	ALL AGES*	OVER 65
	%	%
Cholecystitis and cholelithiasis		
Acute	10.7	21.4
Chronic	0	6.0
Choledocholithiasis	12	12.8

*Zollinger and Young⁸ and Branch and Zollinger.⁹

groups,—acute cholecystitis and cholelithiasis, chronic cholecystitis and cholelithiasis, and choledocholithiasis,—and the mortality rates for each are compared with those for 300 consecutive cases of all ages reported by Zollinger and Young,⁸ and 235 cases of acute cholecystitis reported by Branch and Zollinger.⁹

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The nearly equal mortality rates for cases with stone in the common duct in the two series is probably due to the fact that stones of the common duct, like gallstones in general, occur most frequently in the older age groups. Most of Zol

The type of anesthesia apparently had little or no effect on the mortality. None of the deaths could be attributed directly to the anesthetic. Ether, alone or in combination with nitrous oxide, Avertin or novocain, was the overwhelming

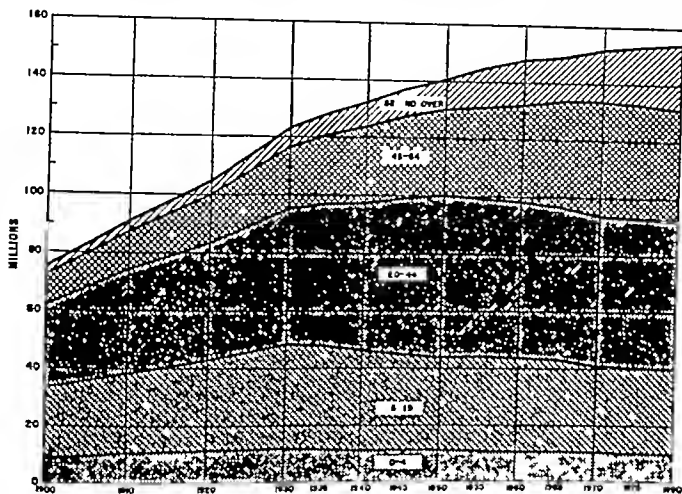


FIGURE 2. *The Trend of Population Change by Broad Age Classes 1900-1980 (Reproduced from The Problems of a Changing Population [Washington 1938] by courtesy of the publisher Government Printing Office)*

inger and Young's patients with stones of the common duct were over sixty years of age.

The mortality in relation to the operative procedure is presented in Table 2. The 4 pa

favorite, being used in 87 cases, despite the fact that it is frequently condemned in the literature on the surgery of the aged. Ethylene and cyclopropane, which are frequently recommended have

TABLE 2 *Mortality in Relation to Operative Procedure*

OPERATION	NO OF CASES	NO OF DEATHS	PERCENT MORTALITY RATE
Cholecystectomy	6	2	30
Cholecystectomy	35	4	11
Cholecystectomy and liver cholecystectomy	4	1	25
Cholecystectomy and choledochostomy	47	6	13
Cholecystectomy	4	0	0
Cholecystectomy	4	0	0

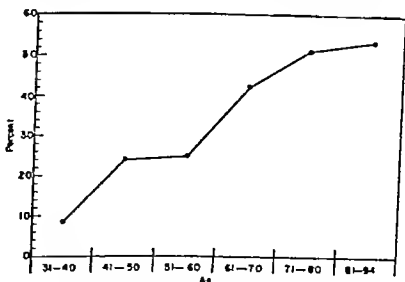


FIGURE 3. *The Occurrence of Gallstones in Relation to Age 1000 routine necropsies (modified from Crump²)*

never been used at the Peter Bent Brigham Hospital

In Table 3 the series is analyzed from the point of view of whether the surgery was elective or

patients on whom exploration of the common duct alone was carried out, and all of whom survived, had been previously subjected to cholecystectomy elsewhere. The presence of jaundice at the time of operation is not in itself a particularly bad omen. Of 46 such patients only 7 died, and none of these died of hemorrhage. In fact one is struck by the absence of emphasis on hemorrhage in the operative notes. This may bear some relation to the fact that no patient in the series who was in good general condition prior to operation was in shock immediately afterward

imperative Only in those cases in which the choice appeared to lie clearly between operation and inevitable progression of the illness was surgery considered as imperative The great majority consisted of cases with acute abdominal catas-

TABLE 3 *Mortality in Relation to Imperative and Elective Surgery*

TYPE OF SURGERY	NO. OF CASES	NO. OF DEATHS	MORTALITY RATE %
MEN			
Imperative	12	7	58.3
Elective	19	2	10.5
WOMEN			
Imperative	17	3	17.6
Elective	52	1	1.9

trophes, acute cholecystitis which failed to subside under conservative general measures and progressive jaundice. The highest mortality occurred among men for whom surgery was imperative Of 52 women for whom surgery was elective, only 1 died

Evidence that the cardiovascular systems of these 100 patients were in excellent condition is shown by their blood pressures These are compared in Table 4 with the figures for corresponding ages

TABLE 4 *Average Blood Pressures Compared to Normal Blood Pressures for Ages Sixty-five to Ninety*

SEX	NORMAL CASES*	CASES IN THIS SERIES	
	mm	LIVING (87 CASES) mm	DEAD (13 CASES) mm
Men	156/70	141/81	153/87
Women	163/89	145/62	144/81

Saller¹⁰ and Richter¹¹

obtained by Saller¹⁰ from a study of the blood pressures of 4000 healthy individuals and with those from a similar investigation by Richter¹¹ of 165 aged men An explanation for the relative hypotension of our patients may lie in the fact that almost none were overweight The average weight for the series was only 136 pounds The relation between obesity and high blood pressure has been well established¹²⁻¹⁴ Chronic biliary disease is not conducive to overeating, and the average duration of symptoms prior to operation in this series was five and a half years However, the 9 men who failed to survive, and who exhibited higher blood pressures than the others, were also somewhat heavier, averaging 155 pounds

Nineteen (22 per cent) of the 87 patients who were discharged well developed postoperative complications Each of the following sequelae occurred once pyelitis, parotitis, wound infection, senile dementia, coronary thrombosis, cardiac decompensation and cardiac asthma Cystitis and protracted vomiting each occurred in 3

patients Three patients exhibited unmistakable evidence of pulmonary infarction, but no deaths from massive pulmonary embolism occurred In 3 patients profound apathy developed Each of these patients had been jaundiced at the time of operation and drained large quantities of bile after it The apathy promptly disappeared when the drainage diminished or bile was administered by mouth Three patients had diabetes mellitus, and 1 of them died Two had pernicious anemia, and both survived operation

The deaths in the series are reviewed in Table 5 In considering the postoperative complications and deaths in these aged patients, one is struck by the remarkable tenacity with which they cling to life. The complications on the whole were minor, and death when it occurred was often late in the post operative period after a long struggle with degenerative disease or sepsis As Rowntree¹⁵ has said, the aged are very often "good livers and take a lot of killing"

COMMENT

Until recent years relatively little was written on the subject of surgery in the aged Morton¹⁶ has properly given credit to the urologists as the pioneers in geriatric surgery They have demonstrated beyond question the value of careful preoperative preparation by reducing the mortality of the formidable operation of prostatectomy to an insignificant figure Aged patients for whom surgery is contemplated fall into two groups, those whose normal routine of life should be disturbed as little as possible during the period of preparation, and those who would be benefited rather than harmed by prolonged rest in bed Sir James Paget¹⁷ recognized these two types when he wrote in 1875

Years, indeed, taken alone are a very fallacious mode of reckoning age it is not the time, but the quantity of a man's past life that we have to reckon The old people that are thin and dry and tough, clear voiced and bright-eyed, with good stomachs and strong wills, muscular and active, are not bad, they bear all but the largest operations very well. But very bad are they, who, looking somewhat like these, are feeble and soft skinned, with little pulses, bad appetites, and weak digestive power, so that they cannot, in an emergency, be well nourished

The cardiovascular and urinary systems must be carefully evaluated in each patient, but evidence of impaired function is not necessarily a contraindication to operation The heart or excretory apparatus that has successfully withstood the insults of seventy years of active duty is often likely to come through a major surgical procedure with flying colors Digitalis should not be forgotten There is no objection to giving the average patient over sixty-five digitalis almost to

TABLE 5 Data on Fatal Cases.

CASE NO.	SEX	AGE	Symptoms	Type of Operation	Anesthetic	Day of Death (Postoperative)	Cause of Death	Pathologic Findings
1	M	75	1 emphysematous pneumonia for 1 yr	Cholecystectomy cholecystectomy	Ether	16	Bronchopneumonia	Marked bilateral bronchopneumonia, bronchiectasis, emphysema, benign hypertrophy of prostate.
2	M	69	Intermittent biliary colic and jaundice for 2 yr. Fever, chills, abdominal distention and jaundice for 8 da.	Cholecystectomy	Narcosis and ether	7	Cardiac failure bronchopneumonia	
3	M	72	Intermittent biliary colic and jaundice for 1 yr	Cholecystectomy cholecystectomy cholecystectomy (14 da. later)	Fiber	120	Subphrenic abscess, empyema	Subphrenic abscess, right empyema per card. act. c. pulmonary tuberculosis.
4	M	75	Indigestion for 8 yr. Abdominal pain, tenderness, and vomiting for 5 da.	Cholecystectomy	Narcosis	8	Cardiac failure bronchopneumonia	
5	M	70	"Indigestion for 2 yr. 3 weeks abdominal pain and protrusion for 8 hr	Cholecystectomy	Ether	1	Cardiac failure	Marked aortic and mitral stenosis and insufficiency, bronchopneumonia, bronchiectasis, pericarditis, benign hypertrophy of prostate.
6	M	67	Biliary colic and jaundice for 2 mo.	Cholecystectomy	Narcosis	3	Bronchopneumonia	Bilateral bronchopneumonia, pneumonia, pericarditis, myocardial infarction, aneurysm of left ventricle, high-grade aortic generalized arteriosclerosis.
7	M	67	Recurrent epigastric pain for 2 mo.; jaundice for 1 mo.	Cholecystectomy cholecystectomy	Ether	18	Right-sided heart failure	
8	M	70	Abdominal pain and vomiting for 9 mo.; jaundice for 3 mo.	Cholecystectomy cholecystectomy (2 da. later)	Ether	4	Cardiac failure	
9	M	4	Abdominal pain increased for 2 wk.	Cholecystectomy	Ether	2	Cardiac failure	Chronic myocarditis, benign hypertrophy of prostate.
10	F	6	"Indigestion for 9 yr.; recurrent one hour jaundice for 1 yr	Cholecystectomy cholecystectomy	Ether	10	Decreasing urinary output	Chronic nephritis. 7 days death.
11	F	1	Abdominal pain, fever and vomiting for 2 wk.; diarrhea with it.	Cholecystectomy (17 da. later)	Ether	10	Septic	Wound infection, subdiaphragmatic abscess, arteriosclerosis, bronchopneumonia, acute splenitis.
12	F	6	Jaundice, chills and fever for 3 wk.	Cholecystectomy cholecystectomy	Ether	19	Left hemiplegia bronchopneumonia	
13	F	0	Recurrent abdominal pain 3 days prior to death for 4 yr	Cholecystectomy	Ether	3	Right-sided heart failure	Marked cardiac hypertrophy, dilated coronary sclerosis.

the point of saturation or of physiological activity prior to operation, so that if signs of decompensation or irregularity of rhythm should appear postoperatively, digitalization can be easily and quickly accomplished. The diet should of course be rich in vitamins and carbohydrates. The liver should be filled with glucose, which can be given conveniently as candy. Jaundiced patients should receive a small intravenous infusion of concentrated glucose on the morning of operation. Alcohol in small quantities has a definite place in the treatment of these patients, both as a food and as a psychological sedative.

Ideally, the operation itself should be an incident in treatment. Morton¹⁶ points out that the delicate technic of Halstead is essential. Rough and bloody operating has no place in geriatric surgery. Old people, like babies, do not stand trauma well. Speed is emphasized by many as of great importance, but, as Rowntree¹⁵ says, an hour of gentle manipulation is far preferable to ten minutes of trauma. Bailey¹⁸ has emphasized the essential fact that the cardiovascular system grows less resilient with age, and that the aged slip into shock more subtly and come out more slowly than do the young.

The type of anesthesia apparently makes little difference. However, as Newton¹⁹ and Rankin and Johnston²⁰ have said, it is essential that it be skillfully administered. Ether, with a minimum of preoperative medication, may often be preferable to local or spinal novocain reinforced by respiratory depressant drugs. Cutler and Zollinger²¹ have called attention to the fact that when novocain is used it should contain no adrenalin, lest angina pectoris or even coronary thrombosis be precipitated. Furthermore, the hemostatic effect of adrenalin is transitory, and its use may be followed by a higher incidence of hematoma formation in the wound. Avertin, as a rule, is unsafe unless given in small doses and syphoned off, as Booth²² has suggested, just before the operation.

Parenteral fluids should be given almost invariably after operation, but not in too great a quantity or too rapidly. An attack of pulmonary edema may be a far more serious ordeal than the operation itself. Morphine and other respiratory depressing drugs should be reduced to the minimum. Atropine is of great value in drying up bronchial secretions and forestalling pulmonary atelectasis and its sequelae. Rankin and Johnston²⁰ emphasize the need of frequent changes of position in bed, deep breathing exercises and carbon-dioxide inhalations. As soon as possible the patient should be out of bed. Sometimes this can

be accomplished on the first postoperative day, but it should never be done when it might prove exhausting. A nice balance must be struck between the patient's strength and the dangers of hypostatic pneumonia.

Finally, the mental attitudes both of the patient and of those attending him are all-important. It has often been said that a surgeon will do well to think, not twice but several times, before operating on a patient who has no desire to live. All too often such patients do succumb, and for no apparent particular reason. The surgeon and his assistants should be cheerful, but not patronizing. The patient's whims should be scrupulously respected, even to the point of disrupting the ordinary hospital and nursing routine. Old people stand regimentation poorly, as Morton¹⁶ has pointed out. Rowntree¹⁵ has phrased the matter delightfully in saying that the aged patient should be treated "physically like a child, but mentally like an emperor."

SUMMARY

The increasing proportion of the aged in the general population is discussed.

One hundred consecutive cases of non-malignant biliary disease in patients over sixty-five years of age, in which operation was performed, are analyzed.

The surgical management of aged patients with biliary disease in patients over sixty-five years

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THE TREATMENT OF HYPOTHROMBINEMIA
WITH SYNTHETIC VITAMIN K₁

Report of Two Cases

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BOSTON

VITAMIN K was isolated by Dam et al.¹ and by Doisy et al.² and was characterized as a quinone by the latter group.³ Fieser et al.⁴ first postulated that vitamin K₁ was 2-methyl-3-phytyl-1,4-naphthoquinone. He synthesized this compound and showed it to be identical with the natural vitamin K₁, which he had isolated from alfalfa. Doisy et al.⁵ independently confirmed the structure of the vitamin. The method of synthesis⁶ has been stated so as to provide a practical source of the pure vitamin in quantity. Fieser reported that this compound had the same degree of activity in chicks deficient in vitamin K as had the natural vitamin, as shown in experiments by W. L. Sampson. The present paper reports the use of synthetic vitamin K₁ in two clinical cases of obstructive jaundice, a preliminary announcement of this study having been made by Fieser.⁶

The prothrombin determination of Quick⁷ was employed. In all tests vacuum sealed portions of the same original preparation of thromboplastin were used. In every determination the activity of the thromboplastin was checked against at least one control. In a series of 75 normal subjects the prothrombin clotting time was found to range between 13.0 and 22.0 seconds. Repeated determinations of the prothrombin time of each normal plasma specimen checked within 10 seconds. In the abnormal specimens the end point was less sharp.

No ill effect was observed in white mice which were fed 10-mg doses of the synthetic vitamin nor in 3 human subjects each of whom was given 20 mg, together with bile, by mouth.

For intravenous use the synthetic vitamin⁸ which is an oil at room temperature, was given as a freshly prepared colloidal suspension in 10 per cent glucose. This solution was prepared by dissolving 10 mg of the oil in 2 or 3 cc. of absolute ethanol and was boiled in order to sterilize the quinone and was slowly introduced, by means of a pipette, below the surface of a well agitated sterile solution of 1000 cc. of 10 per cent glucose in distilled water. The final solution was slightly opalescent. No

particulate matter could be seen microscopically nor was there any tendency for the quinone to separate as an oil, even after standing for several days. Three mice were each given 2 cc. of this colloidal suspension intravenously on one occasion and 2 rabbits were each given 100 cc. of the same solution on four successive days with no untoward reaction. Three normal human subjects were given intravenously 1000 cc. of the freshly prepared colloidal suspension containing 10 mg of the synthetic vitamin; no reaction was noted, and in no case was there a significant change in the normal prothrombin level or in the clotting and bleeding times.

The efficacy of the drug in the treatment of clinical hypoprothrombinemia was studied in the following cases:

CASE 1. I. S., a 67-year-old white tailor entered the hospital on August 9, 1939, complaining of upper abdominal pain of 3 weeks duration. He had noticed darkness of the urine and pallor of the stools throughout this period but was unaware of jaundice. Physical examination on admission revealed evidence of weight loss, marked icterus of the skin and sclerae, ascites and a mass in the upper abdomen interpreted as an enlarged liver. All urine specimens contained large amounts of bile but no urobilinogen. The stools during the first 2 days contained bile pigment, but thereafter the color remained gray or reddish brown. The color suggested changed blood, and repeated guaiac tests were strongly positive. The mercuric chloride test for bile in the stools was consistently negative after the 2nd day. The icteric index on admission was 50; the van den Bergh 8.6 mg. per 100 cc., the cholesterol 337 mg., and cholesterol esters 195 mg. The icteric index rose to 90 in 7 days. Laparotomy was done under local anesthesia on the 15th day. A mass of malignant tissue apparently arising from the gall bladder and involving all the structures of the lesser omentum was found. No curative or palliative procedure was possible. Microscopic examination of a specimen disclosed undifferentiated medullary carcinoma. Postoperatively the patient developed bronchopneumonia and died on the 3rd day after exploration. Permission for postmortem examination was not obtained.

The prothrombin clotting time on admission was 17.0 seconds; within 6 days it rose to 39.5 seconds. The course of the prothrombin clotting times throughout the rest of the study is illustrated in Figure 1 which shows the effect of the oral administration of bile alone, of 10 mg of synthetic vitamin K₁ and bile, and of the intravenous

*Provided through the courtesy of Professor Louis I. Fieser, Harvard University.

⁸See this paper was unaltered the solution has been sterile and 150 p. for 15 minutes without change in appearance, and been found to be effective in the unaltered and too described form.

†Acknowledgment is made to Dr. W. H. Ham, Dana Hall, and Dr. Reginald H. Smith for the opportunity of studying this paper.

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injection of 10 mg of the quinone in colloidal suspension

CASE 2. S F, a 65 year old, white man, with a previous admission 18 months before for coronary thrombosis, entered the hospital on October 2, 1939, complaining of painless jaundice of 5 weeks' duration and pruritus. He had noticed icteric sclerae, darkness of the urine and pallor

of ascitic fluid and an early diffuse peritonitis. Alveoli of carcinoma cells were found in the sediment of the centrifuged ascitic fluid. The cholecystgastrostomy was healing cleanly and had an adequate lumen. However, no bile was found in the gall bladder, stomach or intestinal tract. The gall bladder was shrunken and thin walled, as was the cystic duct. The common duct was dilated, and in its wall an incision was found through which bile was drain-

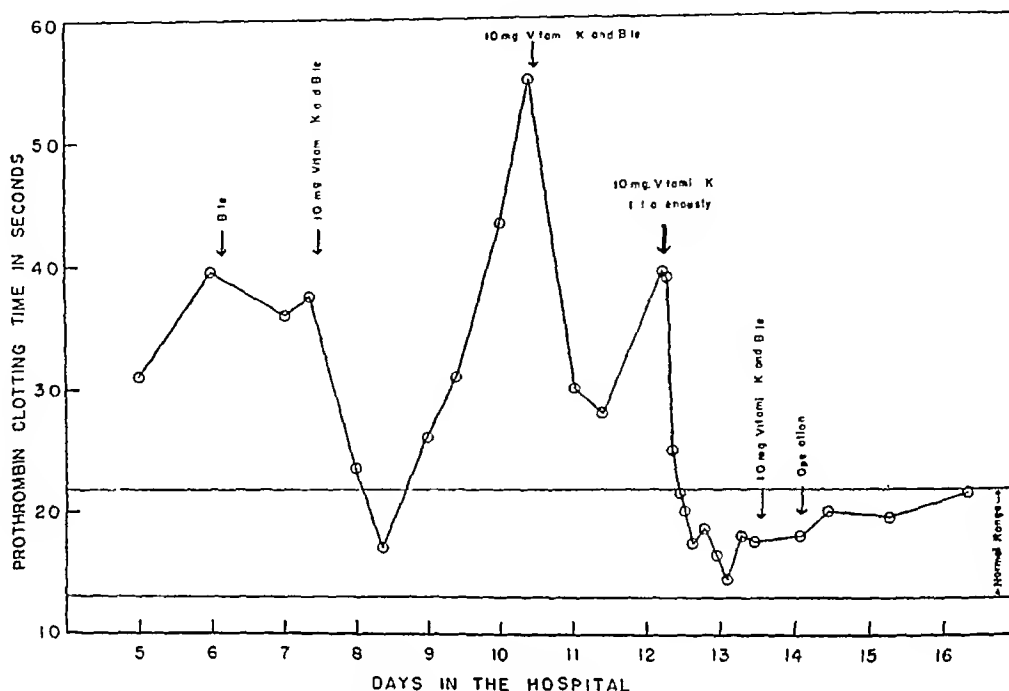


FIGURE 1 Responses in Terms of Drops in Prothrombin Clotting Time Following Oral and Intravenous Administration of Synthetic Vitamin K₁

of the stools throughout this period. He estimated that he had lost 15 pounds since the onset of his illness. Physical examination on admission revealed evidence of weight loss, marked icterus of the skin and sclerae, ascites and minimal pitting edema of the legs. The heart was moderately enlarged, and there were rales and dullness at the bases of the lungs. All specimens of urine contained large amounts of bile but no urobilinogen. During the hospital stay the stools varied in color from light brown to gray. At no time was the mercuric chloride test positive for bile. On one occasion prior to operation the stool showed a positive guaiac reaction. On admission the icteric index was 160, the van den Bergh 25 mg per 100 cc., the cholesterol 211 mg, the total protein 4.4 gm, the albumin 2.7 gm and the globulin 1.7 gm. The icteric index remained between 160 and 170. Laparotomy was performed under spinal anesthesia on the 9th day, and the common duct was found to be dilated and to contain white bile. The gall bladder was small and contained a small amount of light-yellow mucus. The head of the pancreas was firm, suggesting carcinoma, accordingly a cholecystgastrostomy was performed and a catheter was inserted in the common duct. Because of the low serum protein, the patient received a transfusion of 500 cc. of 9-day-old bank blood during the latter part of the operation. During the first night following operation the patient pulled out his common-duct catheter. Thereafter the patient drained moderate amounts of bile but the icteric index, urine and stools remained unchanged. He became increasingly lethargic and died on the 5th day after exploration.

Postmortem examination revealed a moderate amount

ing into the peritoneal cavity. The cystic and common bile ducts were found to run parallel behind the head of the pancreas before joining. Both the cystic and com-

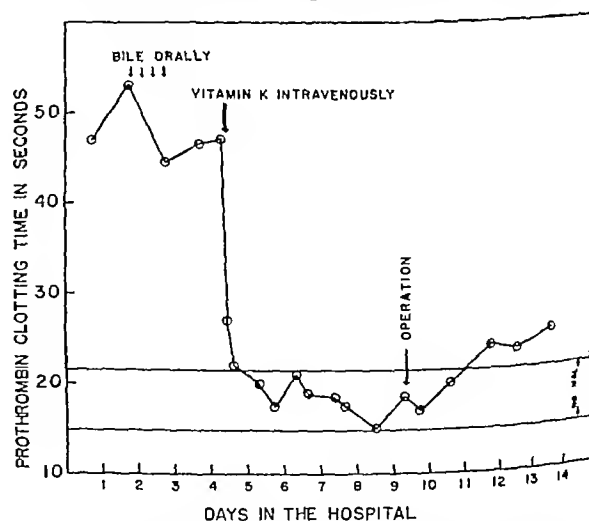


FIGURE 2 Responses in Terms of Drops in Prothrombin Clotting Time Following the Administration of Bile Orally and of 10 mg of Synthetic Vitamin K₁ Intravenously

mon ducts were obstructed at the head of the pancreas, which was firm, nodular and slightly enlarged. Microscopical study of the pancreas disclosed carcinoma.

The prothrombin clotting time on admission was 47.0 seconds. Figure 2 illustrates the effect of a single intravenous injection of 10 mg of synthetic vitamin K_1 on the clotting time as compared with that of 4 gm of bile given orally.

DISCUSSION

In Case 1, a single dose of 10 mg of synthetic vitamin K_1 given by mouth with bile on two occasions to a patient with an elevated prothrombin clotting time produced a drop which was maximal at the end of twenty-four hours. The time rose again in the next twenty-four hour period. As shown in Figure 1 the curve of the activity of the 10-mg dose was similar in shape on both occasions, the starting points being at different levels. Bile alone given by mouth produced no such effect. The intravenous administration of the same dose resulted in a fall to normal levels within four hours, most of the drop occurring within two hours. Twenty-four hours after injection 10 mg of the vitamin with bile was again given by mouth to prepare the patient for operation on the following day. At no time during the operation or in the postoperative period was abnormal bleeding noted. The prothrombin time remained within normal range, without further administration of the vitamin until exitus on the third postoperative day. The results obtained in this case suggest that oral doses repeated at twelve hour intervals might have maintained the prothrombin level within normal limits.

In Case 2, a single intravenous dose of 10 mg of synthetic vitamin K_1 resulted in a fall in prothrombin clotting time to a normal level within four hours. The clotting time remained within a normal range for six days after injection despite

the fact that an operation was performed during this period. Since it is known that the prothrombin content of stored blood falls off rapidly, it is unlikely that the transfusion of nine-day-old blood could have played a significant part in this curve.

SUMMARY

The compound, 2-methyl-3-phytyl-1,4-naphthoquinone synthesized and established as vitamin K_1 by Fieser has been tested for the first time in clinical cases of obstructive jaundice.

No untoward reaction was noted following the oral and intravenous administration of this drug to human subjects or laboratory animals.

A response in terms of a drop in the prothrombin clotting time has been seen to follow the oral and intravenous administration of 10 mg of the synthetic vitamin.

An effective method for preparing the synthetic vitamin for intravenous administration is described.

A single intravenous dose of this synthetic vitamin in two cases resulted in a return to a normal prothrombin level within several hours, and maintenance of this level for several days.

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REPORT ON MEDICAL PROGRESS

THE SURGICAL TREATMENT OF THYROID DISEASE*

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THE title of this report might lead one to the erroneous impression that it represents a review of the literature. This is not its purpose. It is intended to represent my own conclusions and those of the group associated with me in the Lahey Clinic, drawn from an experience with 18,600 patients who have been operated on for goiter. Included in it also are my deductions from the experience of others as reported in the literature particularly as I have applied them in a practical manner to my daily practice with thyroid disease.

While there are those who still wish to employ measures other than surgical in treating patients with toxic goiter, such as rest, psychic management and x-ray therapy, they represent, it seems to me, a constantly diminishing group. Fewer and fewer papers and medical-meeting discussions relating to the non-surgical treatment of toxic goiter are appearing. It may with reasonable safety be said that when a sufficient number of cases have been treated by methods plainly different in their plan, the end results in the minds of the patients and their medical advisers will so settle differences of opinion that there will be but little uncertainty. It must be assumed that no group of 18,600 patients would submit to subtotal thyroidectomy if there were an equally satisfactory method of treatment which did not involve a surgical procedure.

The advantages of the surgical removal of a considerable portion of the thyroid gland in the treatment of hyperthyroidism are that it is possible by this form of treatment to free patients from the undesirable effects of the disease with greater certainty, with more completeness, with fewer recurrences and in a shorter period of time than by any other method. When one realizes the low mortality rate—0.76 per cent in our series—and the fact that the complications such as tetany and recurrent-nerve injury have been virtually eliminated, this conclusion becomes even more definitely established.

We hear very little today concerning patients with toxic adenomas of the thyroid gland, representing a separate group. There is an almost universal tendency to accept cases of toxic thyroid

gland as representing a single disease. Patients with toxic adenoma present two outstanding clinical features as compared to those with true primary hyperthyroidism. First, they respond less well to iodine medication. Second, they show less improvement after preliminary pole ligation and, probably because of their advanced age and the resultant damages to other organs, the operative procedure involves a greater hazard.

There is a tendency to assume that several weeks of hospital preparation are necessary in severe cases of thyroid intoxication. There are, to be sure, patients, particularly those with associated cardiac decompensation and those in states of thyroid crisis, with vomiting and diarrhea, in whom periods of two or three weeks may be necessary for adequate preparation, but our mortality rate was obtained with a period of preparation of from eight to ten days.

It is still necessary to impress upon family physicians the advantages of not administering iodine to patients before sending them to surgeons for operation. One of the questions most frequently proposed to me in discussing this subject in various parts of the country is, What do you do with the patient who comes to you still quite toxic after having received iodine for several weeks, the so-called iodine-fast patient? While no universally reliable rule can be laid down, it is my conviction, after having dealt with hundreds of such patients, that it is very much better to submit them to a reasonably immediate, graded, partial thyroidectomy (pole ligation or hemithyroidectomy) than to send them home off iodine to deiodinize them. If they are in a dangerously toxic state the removal of iodine may intensify their toxicity. If they are not, they will be able to withstand either pole ligation or first-stage hemithyroidectomy, and the progress of the disease in the great majority of cases will then be definitely checked or lessened. We are convinced that a two-stage operation is preferable to the delay involved in attempts so to deiodinize patients that they will again react satisfactorily to iodine.

There is no type of case in which the question of anesthesia is more vital than in the patient with hyperthyroidism. The patient is often in such a precarious state that the balance for or against a fatal termination is tipped by a single factor.

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such as the anesthetic. There is an inclination on the part of some surgeons to assume that local anesthesia decreases the risk of the surgical procedure, particularly in severely toxic cases. This I do not believe to be true. We have experimented with practically all the different forms of anesthesia for patients with toxic thyroid glands and are firmly convinced that cyclopropane, with its very high oxygen content and its powerful anesthetic properties, is by far the best. Ether is undesirable because of its relatively prolonged period of induction with the associated excitation and its tendency to increase postoperative vomiting, a particularly unfortunate complication in the presence of hyperthyroidism. There is nothing better calculated to promote a state of thyroid crisis than vomiting. It prostrates the patient, it adds to the burden on the heart and most unfortunate of all, it prevents the intake of fluid and fuel (food) by which the ravages of the excessive metabolism are at least in part counteracted.

In selecting an anesthetic for a patient with toxic goiter it is important to remember that 250 cc. of oxygen per minute is the normal demand under an anesthetic, while in cases of toxic goiter it may run as high as 800 cc. With these figures in mind as related to nitrous oxide, ethylene and cyclopropane anesthesia, we must recall that the oxygen content of nitrous oxide anesthetic mixtures is only about 9 per cent of ethylene from 15 to 20 per cent and of cyclopropane from 50 to 85 per cent. Having used cyclopropane for the last five years, we are sure that in spite of the hazard of explosion it is by far the best of all the anesthetics for use in the surgery of toxic goiter.

One must not forget that there is just as great hazard of explosion with a mixture of nitrous oxide, oxygen and ether as exists with cyclopropane or ethylene. There have been as many such fatalities with this anesthetic mixture as have occurred with the two hydrocarbon gases named. This sort of fatality is a particularly shocking catastrophe. It requires no investigation to prove the cause of death. The suddenness of the detonation its immediately obvious effects—subcutaneous emphysema from pharyngeal laryngeal and alveolar rupture—and the absolute impossibility of anticipating it are well calculated to throw our judgment concerning it a little out of line. In a calm and unprejudiced consideration of what is best for these patients, we must give thought to how many fatalities of a less dramatic nature have been due to the less obvious cerebral damage occasionally associated with nitrous oxide anesthesia to the subtle but real dangers of low oxygen anesthetic mixtures in the surgery of this disease, to the added technical difficulties result-

ing from this form of anesthetic and to the post operative vomiting caused by it.

My objection to local anesthesia is that patients with toxic thyroid glands are less well able to withstand the emotional ordeal of a major surgical procedure awake and conscious than is almost any other type of patient. We have found that there are no narcotics which can be employed in safe doses and at the same time ensure that the patient will not remain awake and keenly conscious of painful stimuli and of what is going on.

In advocating cyclopropane we must insist that it be administered only by anesthetists familiar with all the necessary precautions against static spark and consequent explosion. No anesthetist should fail to read a recent paper by Woodbridge, Horton and Connell¹ concerning the prevention of the ignition of anesthetic gases by static sparks, and he should familiarize himself especially with the intercoupler described therein which was devised in order to lessen the dangers in the use of explosive anesthetic gases.

Intratracheal anesthesia is one of the most valuable developments of recent years for the patient with thyroid disease requiring surgery. In cases of intrathoracic goiter with tracheal narrowing the introduction of the flexible, rigid walled intratracheal catheter ensures a constant flow of anesthetic and oxygen and permits all the intrathoracic manipulations necessary for its removal without the disadvantages and dangers of tracheal collapse during the operation. Should a patient have difficulty in obtaining enough air while being operated on for toxic goiter he should not be permitted to suffer the ill effects of sub-oxygenation over a period of time, thus adding to the danger of the procedure, but an intratracheal catheter should be immediately introduced. This can be done through the laryngoscope by a competent anesthetist in a few minutes and assures a free airway, a sufficient supply of anesthetic and oxygen and a comfortable and calm time for the surgeon, already disturbed by the obvious risk of the surgical undertaking. Prolonged laryngeal spasm is as undesirable a complication as one can have in the anesthesia and surgery of severe toxicity of the thyroid gland and in a small percentage of cases, due to the added cardiac burden tends to increase mortality. By means of the intratracheal catheter it can be avoided.

In reviewing our fairly large experience in thyroid gland surgery we find that 76 per cent of the patients were toxic, and that the percentage of cases in which multiple stage measures were employed was approximately 22. This rate varies between 20 and 26 per cent from year to year de-

pending on the relative number of seriously toxic patients who present themselves for operation. We have at times diminished this percentage in the fear that we were being overcautious, but whenever we have done so the mortality rate has risen.

Statements have from time to time appeared in the literature and been made at medical meetings to the effect that multiple-stage operations are unnecessary for cases of toxic goiter. This may have been true of the cases reported and of the part of the country in which the operations were done. Nevertheless, if such an attitude were to be universally adopted much harm would result. To compare such a position with ours it would be necessary to make a comparison of cases, an almost impossible accomplishment. One would need to know whether or not the patients were as severely toxic, how long the hyperthyroidism had existed, what the amount of weight loss was, the age incidence, how many patients were in or had had a recent crisis, and numerous other factors which relate to possible mortality. That there are different types of thyroid gland abnormality in different parts of the country has for a long time seemed probable to me and to those of my surgical friends who are constantly dealing with cases of thyroid toxicity. I therefore urge emphatically that each surgeon who operates on such patients arrive at his own conclusions, based on his own experience, ability and equipment and on the type of hyperthyroidism seen in his community. If a mistake is to be made, let it be made on the side of too many multiple-stage procedures rather than on that of too few. This attitude is the one which we have maintained, and is one inclining always toward conservatism and safety. I have repeatedly been convinced from the postoperative course that I could have completed the operation in one stage. How, in the event of the uncertainty as to the outcome, even in the face of this wide experience, could I ascertain it except by committing the patients to the risk of a fatality and completing the operation? A surgeon performs a one-stage subtotal thyroidectomy on a patient with thyroid toxicity for only two reasons: because he is sure that the patient can withstand it, or for the sake of time and expense. To save a patient time and expense by doing one-stage operations for any disease unless the patient is obviously a good risk is the poorest kind of investment, and he who advises it is the poorest kind of financial counselor. One of the things that those of us who are operating on patients with severe thyroid gland toxicity must constantly have in mind is the need of standing firmly against their expressed wish for a one-stage procedure. The surgeon who selects the grade of

operation to fit the patient with thyroid gland toxicity must accept entire responsibility for the outcome. When patients request or demand a one-stage operation this must bear no weight, since they have no knowledge of the risk factors. When patients have said to me, as they repeatedly have, "I shall take all the risks of a one-stage operation," I pay no attention, because I know that what they really mean is, "I shall take all the risks of a one-stage operation provided I do not die." Friends, family, the distance from home, the time away from home and family, and added expense have no place in the decision for or against a multiple-stage operation if a one-stage procedure carries the possibility of a fatality. How frequently has death resulted from a desire on the part of surgeons to save time, discomfort and money! Here is involved that intangible factor called surgical judgment, something that does not lend itself to verbal description. It does, however, lead to decisions in the direction of safety when doubt exists as to the certainty of the outcome.

I have for several years been obliged to set up in our clinic, dealing as it does with so many patients with severe degrees of hyperthyroidism, the most demanding and even harsh standards of responsibility for fatalities. These are well calculated, however, to promote conservatism, to discourage the taking of chances and to accomplish low mortalities. These standards are as follows. Should a patient die following a complete subtotal thyroidectomy, it is the result of an error in surgical judgment, and it is to be assumed that the patient would not have died had the operation been divided into two stages, a first-stage right subtotal hemithyroidectomy, followed in six weeks by a second stage left subtotal hemithyroidectomy. Should the patient die following a right first-stage hemithyroidectomy, this is likewise due to an error in surgical judgment, and it is to be assumed that he would not have died had the procedure been bilateral pole ligation instead of first-stage hemithyroidectomy. Should a patient die following bilateral pole ligation it is to be assumed that he would not have died had one pole been ligated first and the other one a week or two later. These are obviously severe standards, but hyperthyroidism is an uncertain and dangerous disease, capable of producing unexpected fatalities, and a surgical approach is required that is characterized by constant and unvarying caution.

There has been a tendency in recent years to assume, first, that the use of iodine makes pole ligations no longer necessary, and second, that mere ligation of the superior thyroid poles, com-

prising less than half the thyroid blood supply, accomplishes no material result

In answer to the first assumption, of approximately one thousand goiter operations done each year in our clinic, some twenty are pole ligations, done because the patients were considered too ill with hyperthyroidism to withstand a first stage right hemithyroidectomy. While these patients form a relatively small group they are the most severely toxic ones. In most cases the body weight has dropped to well below 100 pounds, and obviously it is in this group that we must most seriously consider the possibility of a fatal outcome.

As to the second assumption Marshall² and I³ have reviewed the cases in which we performed preliminary bilateral pole ligations and those in which we performed right first stage subtotal hemithyroidectomies, with particular attention to the effects of these procedures on basal metabolism, pulse and body weight. Of the cases submitted to bilateral pole ligations there was a drop in metabolism, a drop in pulse and a gain in weight in 66 per cent. Of those submitted to right first stage subtotal hemithyroidectomies there was a gain in weight, a drop in metabolism and a drop in pulse in 85 per cent. These figures speak for themselves. With an operative procedure available as brief and as simple as pole ligation which offers two chances out of three of lessening the risk of a subtotal thyroidectomy it should certainly be employed if there is any doubt in one's mind that the patient can withstand the right first stage subtotal hemithyroidectomy. If there is doubt that a patient can withstand a one stage complete subtotal thyroidectomy, and it is known that an operation taking much less time and of less magnitude (first stage subtotal hemithyroidectomy) offers an 85 per cent chance of marked improvement, thus making the second stage hemithyroidectomy infinitely safer, it should by all means be chosen. Until the mortality of operations on the thyroid gland has reached zero, we must keep in mind the possible need of multiple stage procedures in patients with severe hyperthyroidism.

One of the most serious problems of thyroid surgery concerns how much thyroid tissue should be removed and how much should be left. One should not leave such large remnants that the hyperthyroidism persists or recurs. Neither does one wish to remove such quantities of the gland that myxedema results. There can be no set rule as to how much thyroid tissue should be removed. It is necessary to vary the amount of thyroid tissue with the different types of thyroid tissue involved and by the extent to which in-

volution has taken place following the administration of iodine. Cattell⁴ demonstrated in our clinic some years ago that the degree of involution under iodine varies in different individuals. It is obvious, therefore, that no one fraction of the thyroid gland—three fourths or four fifths or five sixths—can be specified as the proper amount to remove in all toxic cases. There is no place in surgery where judgment based on results obtained from the removal of varying amounts of thyroid tissue is more needed than in decisions as to how much thyroid tissue to take out in a given case.

Determinations of blood iodine which have been carried out in the Research Foundation of the clinic^{5, 6, 7} have proved of great value in showing in what group of toxic thyroid patients the highest percentage of recurrence takes place, and so in what group the most radical thyroidectomies must be done. In 70 per cent of all cases of hyperthyroidism examined it was found that the blood iodine was elevated in proportion to the elevation of the basal metabolism and that following subtotal thyroidectomy when the basal metabolism had reached normal the blood iodine had likewise reached normal. The percentage of recurrent hyperthyroidism in this group was 0.5 per cent. In the remaining 30 per cent of cases, while the basal metabolism was elevated the blood iodine was either normal or below normal. The percentage of recurrent hyperthyroidism in this group was 22 per cent. It is obvious from these figures that blood iodine determinations have a value in indicating in which group of cases recurrences may be anticipated and so in which group more radical subtotal thyroidectomies should be done.

Injury of a recurrent laryngeal nerve produces paralysis of the vocal cords on the side on which the injury occurs. This is not a serious catastrophe, since most of these patients are able to breathe well after this injury, and as soon as the remaining cord compensates by passing over beyond the midline a fairly good voice is acquired. When, however, both recurrent laryngeal nerves are injured a real calamity has occurred. There is at first loss of voice, still with normal ability to breathe, but within a few months, although the voice returns, there is increasing difficulty in breathing because of the constant narrowing of the glottic space from fibrosis of the cords and fixation of the arytenoid cartilages. The glottic space with further narrowing may become so small that the necessity for a tracheotomy is urgent. Until a few years ago there were no operative procedures which were satisfactory for this condition. Two are now available, one devised by Hoover⁸ of our clinic, and proved quite reliable by the test of time (five years) the other devised by

King,⁹ of Seattle, not as yet proved reliable by the test of time but offering the promise of being entirely satisfactory. Hoover's operation consists of the submucous excision of one cord through a laryngofissure, thus leaving an adequate airway, represented by the space in the larynx previously occupied by the removed cord, and, most important of all, a space adequately lined with mucosa. In King's operation the severed omohyoid muscle is sutured into the arytenoid through the thyroid cartilage, and in addition the arytenoid is pinned back to the side of the larynx by a stitch passed around it from the outside. This is an ingenious procedure which offers a distinct prospect of relief for these distressed patients, it has the advantage over Hoover's operation of being performed extralaryngeally and so aseptically. I am extremely doubtful of the efficacy of employing the omohyoid muscle to bring about any coordinated cord action. The value of this procedure is, I believe, largely represented by the stitch which so pins the arytenoid to the side that the cords are held apart at this point.

It has always seemed to me strange that avoidance of the recurrent laryngeal nerve in thyroid operations was accomplished by taking pains not to see it. The plan of avoiding injury to the nerve, by leaving sections of thyroid tissue over the region where it is supposed to be, descended from the original descriptions of the technic of thyroidectomy by Kocher, the father of thyroid surgery. I had for several years thought that such a plan was antiquated and not in accord with the modern conceptions of surgery. I have always taken the position that exposure was one of the funda-

mental principles of surgery, that what one could see he could avoid, and that what one could not see, particularly if it be in the field of operation, one could never be sure of avoiding. With this in mind, I and the other members of our clinic undertook four years ago the dissection and demonstration of the recurrent laryngeal nerves in all operations for goiter in any form. This has been carried out in over four thousand thyroid operations. The procedure, therefore, has been employed in a sufficient number of cases and over a long enough period for us to state with safety that the dissection and demonstration of these nerves result in no changes in the voice, and no obvious changes in the function of the vocal cords. As a result of this procedure the incidence of nerve injury, which previous to the employment of this plan was 17 per cent, has in the last four years dropped to 0.3 per cent, including those cases in which nerves were purposely sacrificed in operations for cancer of the thyroid.

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CASE RECORDS OF THE
MASSACHUSETTS GENERAL HOSPITALANTHEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 2551

PRESENTATION OF CASE

A seventy-seven year-old man was admitted complaining of urinary frequency.

About a year before admission the patient began to have progressively increasing urinary frequency and nocturia, which became much worse one week before entry, so that he urinated once every thirty minutes. He passed only a small quantity at a time, but there was no apparent retention, incontinence or difficulty in starting or stopping the stream. He drank only a few glasses of water a day and denied having had hematuria, dysuria or pyuria at any time. He was confined to bed for a week prior to entry because of extreme weakness and fatigue.

In the past the patient had enjoyed general good health. At the age of forty he had typhoid pneumonia but was well following this illness until two years before admission when occasional palpitation of the heart and slight dyspnea on exertion appeared. Dyspnea sometimes accompanied palpitation and generally occurred in short nocturnal attacks which woke him from sleep. About six months before hospitalization his appetite began to fail so that his diet during the last month of his illness had consisted of little but "toast and milk." Numbness and cramps in both feet and soreness of the tongue were experienced during this time. His best weight two years before admission was 180 pounds, a few weeks before admission he weighed 145 pounds.

He stated that his blood pressure was all right in the past that he had never had swelling of the face, hands, feet or abdomen and that he had never noticed chest pain, hemoptysis or orthopnea. He denied any history of scarlet or rheumatic fever, diphtheria, nephritis or hypertension.

Physical examination revealed an emaciated, thin, pale, drowsy man in no acute distress. The skin was dry, loose and inelastic, the mucous membranes were likewise dry and pale. The breath was not urinous. There were bilateral arcus seniles, the fundi were not seen because of the small size of the pupils. Teeth were absent. The tongue was smooth, shiny and dry. The heart was enlarged to a point in the fifth left

interspace 13 cm. beyond the midsternal line. The aortic second sound was loud and greater than that of the pulmonic. The rhythm was regular, the rate 84 and the blood pressure 150 systolic, 70 diastolic. The brachial and radial vessels were hard and tortuous. The prostate was enlarged to twice its normal size, it was symmetrical, firm but not hard, and the median sulcus was preserved. The lungs, abdomen and the remainder of the physical examination were normal.

The temperature was 99°F., the pulse 92, and the respirations 20.

Examinations of the urine showed specific gravities ranging from 1.010 to 1.013 even after concentration tests had been performed. There was a constant albuminuria ranging from +++ to ++++ and occasional red cells, white cells and hyaline casts in the sediment. The Bence Jones protein test was negative. The blood showed red cell counts from 1,500,000 to 2,000,000 with 38 per cent hemoglobin and a white-cell count of 5000 with 65 per cent polymorphonuclears, the smear revealed much variation in the size of the red cells but few microcytes. Further blood studies showed a corrected hemoglobin of 33 per cent (44 gm.) a red-cell count of 2,000,000 a hematocrit of 25 per cent a color index of 0.83 a mean corpuscular volume of 125 cu. micra (normal 80 to 94) and a mean corpuscular hemoglobin of 22 micromg. (normal 27 to 32). A serum formol gel test gave a ++ reading in one hour. The serum protein was 7.6 gm. per 100 cc., with an albumin of 2.6 gm. and a globulin of 5.0 gm. or an albumin globulin ratio of 0.5. The serum calcium was 9.4 mg. per 100 cc., the serum phosphorus 4.4 mg., and the serum phosphatase 50 Bodansky units. The blood Hinton test was negative. A gastric analysis showed no free or combined acid. After histamine, however, 44 units of free acid were obtained.

Röntgenographic studies of the chest showed the heart enlarged toward the left and calcification of the aorta. There were no definite mediastinal masses. The right third rib was unusually thin and small but of normal length. Plates of the skull showed sharply defined, rounded areas of decreased density in the parietal bones without increase in the vascular markings. However a better x-ray examination of the skull spine and ribs eight days later showed no positive evidence of disease. Rounded areas of rarefaction in the skull were still present but were localized to the upper parietal areas, in which several blood vessels were seen. At the same time, re-examination of the chest showed diffuse disease characterized by small irregularly rounded areas of consolidation. There was also diffuse thickening of the

pleura, without signs of fluid. The lung roots were not unusually large.

The patient failed slowly but steadily. The temperature ran a slightly elevated course around 99.6°F., with three spikes to 102. He was transfused and given a high-vitamin, high-caloric diet, with bed rest and sedation when needed. In spite of all efforts he died quietly on the fifteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR JOHN H TALBOTT. This man, seventy-seven years of age, came to the hospital complaining of frequency and nocturia for a year. He had no retention, incontinence, difficulty in starting the stream, hematuria, dysuria or pyuria. The fact that at seventy he had dyspnea and some palpitation with nocturnal attacks does not impress me particularly. They can probably be attributed to senile changes. In the past he said that he had had "typhoid pneumonia." This diagnosis was frequently made twenty years ago. He may very well have had typhoid fever and pneumonia at the same time. Six months before admission his appetite began to fail. During the month before entry he had eaten nothing but "toast and milk", this is an important observation. He had numbness, cramps, soreness of the tongue and a loss of 35 to 40 pounds in weight. The diseases that came into my mind when I read these statements were carcinoma of the stomach and pernicious anemia. In anyone over the age of sixty who has lost 35 pounds of weight, has no appetite and has been forced to resort to a milk-and-toast diet, we must think seriously of carcinoma of the stomach. On the other hand, the blood findings, numbness, cramps and soreness of the tongue make one think of pernicious anemia. On physical examination it was obvious that he was dehydrated and drowsy but not in acute pain. The absence of pain is significant. The breath was not urinous. I wonder if it would be sporting to ask for the nonprotein nitrogen in the serum?

DR TRACY B MALLORY. It was 47 mg per 100 cc.

DR TALBOTT. It was probably taken on admission and not repeated.

DR MALLORY. Yes.

DR TALBOTT. This information is of little help. In a man of seventy-seven who probably had a generalized arteriosclerosis, a nonprotein nitrogen of 47 mg does not point one way or the other. We are certain that he had renal insufficiency, but the pathogenesis is not clear. The heart was enlarged, particularly the left ventricle, and there was some aortic arteriosclerosis, as well as generalized arteriosclerosis. He had had no hypertension in the past, or on admission. The prostate

was twice the normal size, symmetrically firm, but not hard. If a prostate is enlarged and firm, this may be due either to cancer or to benign hypertrophy. The lungs, abdomen and the remainder of the examination were normal. I am sure they were looking for evidence of passive congestion. There was nothing on physical examination to make this diagnosis. He had no fever, hence it was not an acute infectious episode. The specific gravity of the urine did not exceed 1.013 after concentration tests had been performed. One thing we observe on the wards is that routine specimens frequently have a higher specific gravity than those following a concentration test. I do not know the explanation. Following abstinence from fluid for twelve hours a normal person should be able to concentrate the urine above 1.020. Following abstinence for thirty-six hours on a dry diet a normal person should concentrate above 1.027. I repeat that the specific gravity in this patient was below the average normal range. We cannot disregard the +++ to ++++ albuminuria and the occasional red cells, white cells and casts in the sediment. Bence Jones protein was not found, I do not know whether an isolated specimen was tested or one collected over a period of twenty-four hours. If it were an isolated specimen it would not be so significant as a complete twenty-four-hour one. For some unexplained reason Bence-Jones protein may be excreted only at certain times of the day.

DR CHESTER M JONES. I think it was an isolated specimen.

DR TALBOTT. There was gross albuminuria, and for this reason I should have preferred a test on a twenty-four-hour specimen. A diagnosis of multiple myeloma must be considered in this case. There was a profound anemia, not the so-called hyperchromic anemia but normochromic. The color index was somewhat low. If this were secondary anemia due to bleeding or carcinoma of the colon, we should expect a color index lower than 0.8. The anemia is of the primary type, which is seen in cases with liver disease, carcinomatosis, leukemia and multiple myeloma. The white-cell count was 5000. I wonder whether this leukopenia was re-checked.

DR JONES. At a second determination it was 4500.

DR TALBOTT. That is significant. With a leukopenia, aleukemic leukemia and cirrhosis should be considered. The mean corpuscular volume was below normal, but the record implies that the cells were larger than normal as indicated by the macrocytes. The mean corpuscular hemoglobin was below normal. The serum formol-gel test is an index of the amount of globulin or euglobulin

resent and is negative in a normal person. This patient had a ++ reading in one hour. I am uncertain about the interpretation of this observation. If the globulin were increased significantly, the test should have been positive in five minutes. The albumin-globulin ratio was reversed, a fact which implies that considerably more globulin was present than albumin. We find such a reversal of the ratio in cases with multiple myeloma. We see it in cases with various forms of liver disease, particularly cirrhosis, but also metastatic involvement of the liver, catarrhal jaundice and obstructive jaundice. The serum calcium, phosphorus and phosphatase were normal. The punched-out areas of the skull makes us think of hyperparathyroidism. We do not think of it for too long a time, however. With this degree of involvement in hyperparathyroidism we should find a higher value for calcium than 9.4 mg. The gastric analysis gave free acid fasting but 44 units after histamine. This helps to exclude a diagnosis of pernicious anemia. Cases have been reported when hydrochloric acid was present, but these are unusual. The presence of free acid in the stomach also helps to exclude carcinoma of the stomach, although 15 to 20 per cent of such cases may have hydrochloric acid.

Dr. RICHARD SCHATZKI. Most of the films were taken with a portable machine, but there are one or two fairly good ones taken in the department. The skull shows multiple, small round areas of increased density in the parietal bone, as described in the report. They are all localized in the parietal region, and I think therefore not so important as if they were elsewhere. We commonly see similar lesions produced by deep Pachionian cysts in this area. From the skull films alone, knowing nothing about the history, I should have to say the findings do not prove a destructive lesion of the bones of the skull although they are certainly much more marked than those we see in the average patient.

Dr. TALBOTT. The man is seventy-seven. Does that make any difference?

Dr. SCHATZKI. No.

Dr. TALBOTT. There was nothing in the pelvis?

Dr. SCHATZKI. No. This film does not prove much in regard to myelomatous lesions because it was probably taken without the Bucky diaphragm. There is very little contrast. We shall discard it. The bones show very many degenerative changes such as you would expect in a man of his age. I do not see any definite areas of bone destruction. I do not see any evidence of marked generalized decalcification, which at times is the only sign of extensive involvement of the bones by multiple myeloma.

Dr. TALBOTT. The third rib on the right shows some abnormality.

Dr. SCHATZKI. There is something definitely abnormal. I believe it is a congenital anomaly.

Dr. TALBOTT. The report reads that "re-examination of the chest showed diffuse disease characterized by small, irregularly rounded areas of consolidation."

Dr. SCHATZKI. The first plate is normal and so is the second plate taken six days later if you discount the different technic. You can see multiple linear markings in both lung fields in a patient with a large heart and a tortuous aorta. I should think they are fibrotic changes of some kind. You see that not infrequently in a patient who has been repeatedly decompensated in the past. It has nothing to do with the present disease. I cannot see any evidence of rib destruction.

Dr. TALBOTT. On the basis of the description in the abstract particularly in view of Dr. Schatzki's opinion, one is foolish to read into the films more than exists, and I do not see how one is justified in making a diagnosis of metastatic involvement of the bones. There are three areas—the skull, the rib and the chest—for possible metastatic involvement, but I should like to have further support or better evidence from the x-ray department before I call any one of them significant.

This narrows the field. Is this a case of carcinoma of the stomach? The man had weight loss, loss of appetite, weakness and fatigue and was on a milk-and-toast diet for a month before he came in. If we had little besides these facts plus the anemia, I should be in favor of making a diagnosis of carcinoma of the stomach. Did the stools show any blood?

Dr. JONES. They were all negative.

Dr. TALBOTT. It is difficult, then, for me to believe this anemia is caused by bleeding from a carcinoma in any part of the gastrointestinal tract. Furthermore, it is unusual to find this much anemia with chronic nephritis without more evidence of the primary disease. Cirrhosis of the liver has not been excluded. We have three things that go with cirrhosis of the liver—an increase in serum globulin, leukopenia and loss of appetite. However, he had no ascites and no jaundice.

In conclusion we have little positive evidence that helps us make a diagnosis. I am more interested in attempting to sum up available data than I am in making an unusual diagnosis. I am always pleased when I make a correct diagnosis of an unusual malady but I do not feel justified in making a guess in this instance. If the roentgenologist will not make a commitment

in favor of metastatic bone disease, then I cannot I am forced to say, then, that this man had only the chronic degenerative diseases that are associated with age, namely generalized arteriosclerosis, chronic myocarditis and chronic nephritis. I do not think he had any of the unusual types of disease that we have discussed.

DR JONES: I am delighted to hear Dr Talbott end up that way. I went through the same line of reasoning. I thought he had what Dr Frederick C Shattuck used to call a mortal disease. He was seventy-seven and obviously was going to die. I was not sure what he had, but in the first few days it was reasonably apparent that he did have arteriosclerotic changes, with cardiac and renal involvement. I thought the patient had what we used to call "cardiorenal disease." The only thing that was difficult to explain was what Dr Talbott has spent a certain amount of time on—anemia which was out of proportion to anything else that we could demonstrate. Any attempt to put it on a nutritional basis was not entirely satisfactory. He was active until a few months before death, when he went to bed. By the time he reached the hospital he was really too sick for us to carry out adequate studies, and that is why, unfortunately, we did not have careful x-ray studies. Dr John Maier insisted from the start that the anemia was not pernicious anemia, since the patient had hydrochloric acid, he wanted to go on record that he might have multiple myeloma as a logical explanation for the anemia. That was the reason for the determination of the albumin-globulin ratio and for the x-ray films of the different bones in the body. He was discharged at death with a diagnosis of chronic nephritis, which was the presenting feature, arteriosclerotic heart disease, and a question of metastatic malignancy or multiple myeloma. Dr Maier was the only one who had the courage to stick to the last diagnosis from the start.

CLINICAL DIAGNOSES

Chronic nephritis
Arteriosclerotic heart disease
Metastatic malignancy?
Multiple myeloma?

DR TALBOTT'S DIAGNOSES

Generalized arteriosclerosis
Chronic myocarditis
Chronic nephritis

ANATOMICAL DIAGNOSES

Plasma-cell myeloma, diffuse
Myeloma kidneys
Polyp of duodenum

Pulmonary tuberculosis, healed, apical
Arteriosclerosis, aortic and cerebral, minimal

PATHOLOGICAL DISCUSSION

DR. MALLORY: The gross postmortem examination failed to tell the story. He had a hypertrophied heart, weighing 470 gm, and slightly small kidneys, weighing 250 gm. The duodenum contained a rather large, flat polyp, obviously benign. The calvarium showed a number of small translucent areas, probably resulting from Pacchionian granulations as Dr Schatzki suggested, which virtually may be considered congenital anomalies and of no significance. Grossly we could make out no areas that suggested tumor in the skull. The bone marrow of the vertebra was very red and a little suspicious. When we cut into the bone marrow of the long bones, it was bright red and hyperplastic. We made a guess at that time that we were dealing with multiple myeloma. The sections showed very diffuse involvement of the bone marrow with plasma-cell myeloma and also quite typical myeloma kidneys, kidneys in which almost every tubule contained a very dense and large hyaline cast. Occasionally these casts are surrounded by foreign-body giant cells. One can frequently make the diagnosis of multiple myeloma merely by looking at the section of the kidney. The liver and spleen contained a good many abnormal blood cells, readily explainable, I should think, as manifestations of compensatory extramedullary hematopoiesis. The bone marrow had been so extensively replaced by tumor that he was beginning to form some blood cells in the liver and spleen.

CASE 25512

PRESENTATION OF CASE

A forty-eight-year-old married Jewess was admitted because of queer actions and speech.

She had been in excellent health until four months before admission, when she became unusually irritable and cross after her husband had lost his job. Since that time she had gradually lost about 25 pounds in weight. Ten days prior to entry she fell from a stepladder in her home. She was alone at the time and was found an hour later sitting on a chair, complaining of injury to the right shoulder which prevented raising the arm above the head. It was not known whether she was unconscious at the time of the fall or afterward. One day after the fall she complained of bilateral frontal headache, which persisted until entry. On the same day she returned from a shopping tour crying and a neighbor reported that

she had entered the wrong house thinking that it was her own. One week before admission her husband noticed that she was acting queerly. She would stare straight ahead, and it was difficult to attract her attention. She had had defective hearing for fifteen years, but it had suddenly become much worse and in order to make her hear one had to shout. She complained of roaring in her head and asked her husband if he heard the noises. On one occasion while walking with her sons she said that she did not know where she was. One day later on getting out of bed she exhibited a staggering gait. She had forgotten a visit of her son a half hour after he had left. When asked how many children she had she replied "five," but could name only three of them. She had had four, but one had died of diphtheria at the age of three. When taken to the bathroom she was unable to find her way back to her room. She rapidly forgot things that she had said. Five days before admission she entered the Emergency Ward where examination showed no abrasion or discoloration of the forehead but slight tenderness on pressure over the mid frontal region. Examination of the fundi showed indistinct disk margins, but the disks were not elevated. There were no neurological signs. A lumbar puncture showed normal pressure and normal fluid. She was discharged with a diagnosis of concussion. Two days later she vomited twice and on the following day reentered the Emergency Ward complaining of frontal headaches and noises in her ears.

Physical examination showed a well-developed and nourished woman with a dry skin. She had an almost constant smile, was deaf and replied to questions irrelevantly, usually in a whisper. She could not name objects held before her but could say for what they were used. She knew that she was in a hospital and talking to a physician. She understood only the simplest of commands, such as "sit up." When asked to touch her ear she touched her nose. To nearly all questions she gave her first name as an answer. When a pencil was put in her hand and she was told to write her name she did so, but if the pencil was handed her upside down she tried to write without turning it around, unaware that she was not making a mark. She could not read. When asked her name she gave the right first name but the wrong name. A Barany chair test showed normal caloric reactions and nystagmus. A caloric test gave equal reactions on both sides. The pupils reacted slightly to light, better to accommodation. The fundi showed no definite abnormality. She could see fingers at a distance of 6 feet. There was a right homonymous hemianopsia. The ears showed no visible abnormality. All her teeth had

been removed. Examination of the chest was negative. The blood pressure was 120 systolic, 78 diastolic. The reflexes were active and slightly greater on the right. The Babinski signs were negative.

The temperature was 98°F., the pulse 68 and the respirations 20.

A urine examination was negative except for the presence in the sediment of 25 white cells per high power field. The blood showed a red-cell count of 5,100,000 with 90 per cent hemoglobin and a white-cell count of 9050 with 64 per cent polymorphonuclears. A blood Hinton test was negative. A lumbar puncture showed normal pressure, normal dynamics and a clear colorless fluid with 6 polymorphonuclears per cubic millimeter, the total protein of the fluid 22 mg per 100 cc., the sugar 72 mg., the gold sol curve 0100000000 and the Wassermann test negative. X-ray films of the skull and chest were negative.

On the eighth hospital day there was slight right facial weakness and the triceps, ankle and knee reflexes were slightly greater on the right than on the left. There was an equivocal Babinski on the right. She became increasingly restless and unco-operative. On the twelfth hospital day all the deep reflexes were greater on the right than on the left. The Babinski was equivocal bilaterally. A Hoffmann sign was elicited on the left. The temperature, pulse and respirations remained normal. On the twenty-fifth hospital day a lumbar puncture showed an initial pressure of 150 mm of water, the fluid contained 17 lymphocytes and 25 red cells per cubic millimeter and showed a total protein of 31 mg per 100 cc., a sugar of 72 mg., and a normal gold sol curve. On the twenty-eighth hospital day the patient was found rigid, breathing stertorously with frothy saliva coming from the mouth. The arms and legs were extended with marked rigidity at the elbows and knees. The wrists were uninvolved. The neck was moderately stiff. The pupils were dilated to 6 mm., equal and unresponsive to light. The right eye was turned out, the left was in the midline. The fundi showed blurred margins. The reflexes were increased. The Babinski signs were positive on both sides. A lumbar puncture showed an initial pressure of 80 mm, the fluid contained 25 lymphocytes, 4 large mononuclears and 125 red cells per cubic millimeter and had a total protein of 33 mg and a sugar of 101 mg per 100 cc. The temperature rapidly rose to 105.8°F., and she died on the twenty-ninth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. HENRY R. VIETS. We are unable to evaluate this patient's irritability because the husband had

lost his job at the same time. The loss of weight, however, is considerable and cannot be disregarded. The fall may or may not have been important. We cannot tell from the history whether she was unconscious or how severe the fall was and therefore we have to keep that in mind without estimating the importance of it. She began to have frontal headache and then she became confused. She had attacks which seemed to be *petit mal*—she stared straight ahead and her friends could not attract her attention. There was tinnitus, she lost her way, had a staggering gait and had amnesia, so that she rapidly forgot things. She continued to have a headache in the mid-frontal region. In other words in a few days, a week or more, there were developing signs of intracranial disease or of increasing intracranial pressure, it is not clear which. The pressure in the spinal fluid being normal and the fluid being normal, the hospital physicians were probably justified in making a diagnosis of concussion and allowing her to go home. However, she came back promptly with more symptoms.

"When a pencil was put in her hand and she was told to write her name she did so, but if the pencil was handed to her upside down she tried to write without turning it around, unaware that she was not making a mark." It is a question whether she had sensory aphasia and misunderstood commands or did not know how to carry out the movements. One cannot say whether she had partial apraxia or not. When a pencil was put in her hand she did understand. So she did not have true apraxia because she knew the use of the object and could write. When the pencil was turned upside down she did not turn it up and went on writing without making a mark. In other words she did have some apraxia. When you are dealing with a patient who has sensory aphasia and also auditory aphasia, that is, is unable to understand what you want her to do, a difficult diagnostic point is raised. In this case one cannot be sure of the diagnosis because the picture is mixed.

"There was right homonymous hemianopsia." That is the first sign we have pointing to a localized lesion on the left side of the brain between the chiasm and the occipital lobe.

"A lumbar puncture showed normal pressure." That is the third time our attention has been called to that. When one gets only polymorphonuclear cells in the cerebrospinal fluid one immediately begins to think of brain abscess. The total protein was 72 mg per 100 cc. So the lumbar puncture was negative except for a few polymorphonuclear cells and an increased protein. One would hesitate a good deal about making a diagnosis of brain abscess on a fluid as nearly normal

as that, yet it is suggestive and we might keep it in mind.

The lesion on the left side apparently began to increase, for there was a beginning facial paralysis on the right, and something suggestive of a Babinski sign on the right. In other words there was an expanding or encroaching lesion, perhaps not expanding because we still know the pressure was normal, but encroaching, on the left side of the brain, with right homonymous hemianopsia, presumably in the region of the temporal lobe. There again we have the association of this finding with aphasia, which would go with the same localization. On the twelfth day the reflexes were greater on the right than the left and the Babinski was positive bilaterally.

There was no fever or other signs to help in the diagnosis. The next lumbar puncture I should consider normal, although possibly the cell count is on the edge of being high, with 17 lymphocytes. In other words we have changed the formula of the cells from 6 polymorphonuclears to 17 lymphocytes and 25 red cells. We are getting away from the diagnosis of brain abscess to that of some other lesion, there is, however, no evidence of meningitis.

On the twenty-eighth hospital day the patient was found rigid, breathing stertorously with frothy saliva coming from the mouth and so forth, all of which speaks for a fit of epilepsy of some sort. The arms and legs were extended, with marked rigidity at the elbows and knees, the wrists being uninvolved. She had stretching out of the arms and legs, with no description, to be sure, of the head, but something suggesting a cerebellar fit, an observation which tends to localize the lesion in another area from that which we are considering as a possibility. That, however, is not definite enough I think to be of value in localizing the lesion. The right eye turned out, a sign which I think is suggestive of a cerebral lesion.

It was pointed out, and we must not forget, that she had lost 25 pounds in weight in the four months before entry, this is rather suggestive of malignant disease. In regard to the fall, we cannot say anything about the trauma as an etiologic agent, but it might well be the cause of death and might well have activated something there. We simply have no data to go on. She was found some time after the onset of the attack, and we do not know whether she was unconscious and, if so, how long. She did have some cerebral upset because she had a headache the next day and this persisted. Then she began to have convulsions and gradually we begin to develop the idea that she had something on the left side of the brain in the temporoparietal re-

gion, a lesion that appears to have grown greater as time went on, but one which did not cause an increase in pressure. It might have been some lesion that destroyed as it expanded or one that was flat in type and therefore did not displace the brain to any great extent. The other signs simply tell us that the lesion presumably was in this region but do not help in regard to the diagnosis of what the lesion was.

What shall we consider as possibilities? Extradural hemorrhage does not seem likely the course was too slow.

DR. CHARLES S. KUBIK. We later obtained a history of mental disorder and impaired memory before the fall.

DR. VIETS. That might be helpful. I did not want to put too much stress on the fall, but we have to consider it because if we exclude extradural hematoma, we must still think of subdural hematoma. This is the sort of thing that she may well have had, a subdural hematoma in which there is a relatively slight and slow extension of the tumor. The common localization is over the temporal lobe going on to increased signs but again there is a lack of increased pressure, which certainly ought to be found in the final cerebrospinal fluid if not in the earlier one. Moreover, I am certain that if a subdural hematoma had been suspected the diagnostic test of trephining would have been suggested and carried out. I take it that was not done?

DR. KUBIK. No.

DR. VIETS. Then we must consider the possibility of brain abscess. We have cells in the spinal fluid, with normal pressure, protein and sugar and symptoms and signs of an expanding lesion. If it proves to be a case of brain abscess of the temporoparietal lobe on the left side, I shall be greatly surprised. Moreover, there is no preceding history of infection.

Something has affected the brain on the left side and destroyed the tissue in a progressive manner, without expanding as a localized tumor would. My best diagnosis is a metastatic lesion of the brain possibly a carcinoma. Along this line, the loss of weight is suggestive.

CLINICAL DIAGNOSIS

Schilder's disease

DR. VIETS'S DIAGNOSIS

Metastatic brain tumor

ANATOMICAL DIAGNOSIS

Glioblastoma multiforme, bilateral

PATHOLOGICAL DISCUSSION

DR. KUBIK. This patient was in the hospital when I was on service, and it is somewhat embarrassing for me to have the case brought up. Because of the fact that there had been change in personality and impairment of memory some time before the fall, I believed that the fall probably had nothing to do with the symptoms and because the pressure and total protein were always normal, and because of the hemianopsia and impairment of vision and finally the development of what we thought were bilateral signs, I thought that the condition was probably Schilder's disease. The question of an encephalogram or ventriculogram was considered several times, but we always decided against it. We thought we ought to observe the patient a while longer. Then the condition very rapidly became much worse, and there was no point in going ahead with any further diagnostic tests.

Autopsy revealed a very diffuse pinkish-grey tumor which extended bilaterally around the posterior horns of the lateral ventricles and forward into the temporal and parietal lobes, with the greater involvement on the right side. There was very little enlargement or distortion of the ventricles. In the gross there seemed to be two separate tumors, one around the posterior horn of each ventricle. Microscopic sections, however, showed tumor cells extending all the way from one side to the other through the posterior part of the corpus callosum. Histologically the tumor is composed predominantly of fusiform cells, there are numerous mitoses, and I should classify it as glioblastoma multiforme.

A PHYSICIAN. What is Schilder's disease?

DR. KUBIK. Schilder's disease is a degenerative disease of unknown etiology affecting chiefly the white matter, most commonly the large body of white matter in the occipital and temporal lobes. Other parts of the brain or the optic nerves may also be involved.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY
THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

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SUBSCRIPTION TERMS \$6.00 per year in advance postage paid for the United States Canada \$7.04 per year \$8.52 per year for all foreign countries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon on Saturday

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COMMUNICATIONS should be addressed to the *New England Journal of Medicine* 8 Fenway Boston Massachusetts

A MERRY CHRISTMAS

FOR a hundred and twenty-seven years the *Journal*, whether as the *New England Journal of Medicine and Surgery* and the *Collateral Branches of Science*, the *Boston Medical Intelligencer*, the *Boston Medical and Surgical Journal* or the *New England Journal of Medicine*, whether in cold type or in warm spirit only, has been wishing its readers a Merry Christmas!

Our journal's generations of readers, during this course of years, have seen a good many Christmases added to the record, a good many—the majority, we hope—sufficiently merry, and others not so merry in the festive sense of the word. The first readers of the infant *New England Journal of Medicine and Surgery and the Collateral Branches of Science*, to repeat the full title, started perusing this literary prodigy in the midst of an unpleasantness with England that turned out more merrily

for us than for Merry England. How long the issue of the conflict remained in doubt our historical memory fails to announce, but perhaps it was a foregone conclusion by December of that year.

From the War of 1812 on, our recurring periods of financial panic and depression must at times have taken the edge off any contemplated observance of the gladsome Yuletide, and our grim years of civil war saw many an empty stocking and many a vacant chair by the hearth on Christmas Day. As a matter of further record, many of the last twenty-five years have not been uncommonly merry in the usual meaning of the word, what with war, pestilence, panic, depression and again war to complete the cycle.

Why, then, a Merry Christmas? The wish seems a contradiction in terms unless we can find some different definition for the word "merry", some particularly thoughtful interpretation of the whole phrase.

A Merry Christmas, according to the interpretation that we should prefer, is a reaffirmation, regardless of material circumstances, of our faith in the ultimate triumph of those human qualities that Christ crystallized in his teachings and exemplified in his life. The louder the roar of the cannon and the blacker the blasphemies of Antichrist, the more peaceful and the brighter must appear by comparison the spiritual resolutions that we renew at this time.

And so the *Journal*, with special emphasis, again wishes its readers a Merry Christmas in the true universal meaning of the term—a meaning acceptable to all races and faiths and creeds!

THE NATION LOOKS AT SEX

THE United States Public Health Service, having declared itself on syphilis in no uncertain terms, is now formulating plans for extensive sex education projects. This stand has been taken and broadsides have been launched against that which usually is, no matter how we may try to side-step the issue, a result of sex indulgence. The proposed plans are to go to the root of the matter,

and if sex cannot be eradicated it will at least be brought into the light.

One notable objective was attained in the campaign against syphilis—a campaign which is not over, and one in which the Public Health Service provided some of the heaviest artillery—when that enemy was brought into the open and tagged by name. It is a help to know what we are talking about and to be able to wrestle with our problems on the turf instead of in the underbrush and in this light it was of considerable assistance when a rather inconsistently stonemason press broke down and hisped the horrid syllables in black and white. Now, we presume, if sex is to be beaten from its covert, the statutory offense must give way before some Anglo-Saxon equivalent.

Most of us, no doubt, have long believed in sex education of the reasonably young and many of us have tried our hand at it in the privacy of the home or the sanctity of the office. We have learned that it is not so easy to reach the mark in a natural and nonchalant fashion nor are our targets always vulnerable. The very young are not interested in the problems of sex, and the rather older already know too much to be receptive. It is a trick to catch them at that expectantly open minded age and to "give them the works," as the quaint expression goes, so that the information will get across in a reasonably dignified manner.

According to the federal health authorities, sex education in the true sense can be taught in schools only as part and parcel of all the courses in the curriculum. The sex-education course is neither sufficient nor desirable. The emotional and social implications of the subject are as important for young people to know as are the physiological facts.

The question that we should raise, freely granting the high desirability of an understanding of sex with all its implications, concerns the methods by which it can be taught. Can we count on the Latin, the history and the shorthand teachers to do their bit with a clear appreciation of the matter in hand? What are the qualifications of these individuals for dealing with a problem that so often baffles thoughtful parents and patient physi-

cians? If the Public Health Service can tell us how it should be done, then another tally can be chalked up for paternalism in government.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., Secretary
330 Dartmouth Street
Boston

POSTPARTUM HEMORRHAGE FOLLOWED BY A FATAL GAS BACILLUS INFECTION

Mrs. H. W., a thirty-three year-old para III entered the hospital July 22, 1933, in mild labor at full term. On admission the cervix was well taken up and dilated to admit one finger, the breech presenting in left position and just above the level of the ischial spines. The patient continued in poor labor throughout the day, at 12.30 a.m., July 23, the cervix was almost fully dilated, and the membranes ruptured spontaneously at 2 a.m.

The family history was not obtained. The patient's past history was not remarkable. An appendectomy was performed in 1920, and the tonsils and adenoids had been removed in 1925. The patient's two previous pregnancies were normal throughout. Catamenia began at fourteen, were regular with a thirty-day cycle and lasted three to four days. The last menstrual period was October 14, 1932, making the estimated date of confinement July 8. The pregnancy ran a normal course save that there was a tendency to gain weight rapidly. Two attempts were made at external version during the puerperium, but neither was successful.

The patient was a moderately obese woman in apparent good health. The temperature was 99°F., the pulse 80, and the respirations 25. The lungs were normal to percussion and auscultation; the heart sounds were regular, with the apex beat in the fifth interspace and no murmurs. The abdomen was rounded, and the uterus consistent in size with a full-term pregnancy. The position was LSA and the fetal heart rate 140 heard best in the left lower quadrant of the abdomen. The breech was floating. No vaginal examination was performed. The blood pressure was 130 systolic, 68 diastolic, and the hemoglobin 84 per cent (Dare).

The cervix remained at almost full dilatation for

A series of selected case histories by members of the section will be published weekly. Comments and questions by members are welcomed and will be discussed by members of the section.

three hours without progress. In view of this it was decided to perform a breech extraction under nitrous oxygen and ether anesthesia. Under aseptic precautions the frank breech was converted into a footling by Pinard's maneuver. The extraction continued without difficulty until the shoulders had reached the outlet, at which time there was some difficulty in delivering the anterior shoulder under the arch. This having been accomplished, the head was flexed and readily delivered by suprafundic pressure. The child was a normal male infant, weighing 9 pounds, 3 ounces, and cried immediately.

Immediately following the birth of the child there was an abnormal amount of flowing. By Credé's maneuver the placenta and membranes were expressed complete and without difficulty five minutes following the birth of the child. The uterus contracted well following the intramuscular injection of posterior pituitary extract, but flow from the vagina continued. The cervix was then inspected, and it was found that there was a deep bilateral laceration of the cervix, which was most marked on the left. This was repaired with interrupted No. 1 chromic catgut sutures. In spite of this repair the flow was still abnormal in amount. The uterus by this time seemed relaxed and atonic, and on this account it was packed with gauze. This controlled the hemorrhage, and the patient appeared in excellent condition except that the pulse had risen to 140 and the blood pressure was 65 systolic, with a diastolic level that could not be definitely obtained.

At 8.30 a.m. the patient was transfused with 500 cc of citrated blood from a compatible donor. She was also given 1200 cc of 5 per cent glucose solution in saline, intravenously. Despite the transfusion and intravenous medication the systolic pressure did not rise above 90 and the diastolic was obtained at 60. The pulse gradually rose to 160. The patient had slight air hunger but was able to take fluids freely.

At 2.30 p.m. the blood pressure was 80 systolic, 50 diastolic. It was noted that the abdomen seemed distended, and the temperature was reported as 103°F (axillary). The air hunger disappeared, and the patient's color improved. There was no increased amount of staining through the pack, and no evidence of fluid in the abdomen could be made out. The patient was then seen in consultation. The consultant was of the opinion that the picture was one of shock and hemorrhage and that there was the possibility of intra-abdominal bleeding through the cervical wound.

Under nitrous oxide and oxygen anesthesia the

vaginal and intra-uterine packs were removed. There was a slight musty odor noted when the intra-uterine pack was removed, but no definite significance was attached to this. On examining the cervix it was found that although it had been sutured on both sides there was still, on the left above the topmost suture, a laceration about 2.5 cm in length which extended up into the left broad ligament. The patient at this time was not bleeding. The consultant advised that the abdomen be opened, and on so doing enormous distention of the intestines, with some serous fluid in the peritoneal cavity, was noted. There was some edema and induration of the peritoneum of the left broad ligament directly over the laceration of the lower segment. There was, however, no tear into the peritoneal cavity. The consultant advised that the uterus be removed to control any further hemorrhage, and a supravaginal hysterectomy was done without difficulty. During the course of the operation the patient was given two 500-cc transfusions of citrated blood. The pulse dropped to below 140, and the patient seemed in better condition at the end than at the beginning of the operation.

Her condition continued to be poor, and the pulse remained elevated. The temperature gradually rose to 105°F at 7 a.m., July 24. Because of the peculiarity of the postpartum course, the uterus had been sent to the pathological laboratory for culture, the report raised the question of gas-bacillus infection. The patient remained unconscious, the pulse became more elevated and the temperature rose to 107°F (axillary). At 10 a.m. the patient expired, approximately thirty hours following delivery. An autopsy was refused. Blood taken from the heart post mortem yielded cultures positive for *Clostridium welchii*.

Comment. This case illustrates postpartum hemorrhage from a lacerated cervix and its treatment. It also shows the precipitous course of fatal gas-bacillus infection. It is uncommon for a cervix to be torn in breech delivery when practically complete dilatation has been obtained before operation. Proper treatment rests on an intelligent diagnosis. In this case it was immediately ascertained that the cervix was torn and proper treatment was instituted at once. The hemorrhage was controlled, and the loss of blood made up by citrate transfusion. The continued hemorrhage from the atonic uterus was controlled by packing. It is barely possible that the introduction of the pack may have been the means of infecting the patient with *Cl. welchii*. In cases of extreme postpartum hemorrhage, one may see a moderate rise in temperature, but a sustained

nse, such as this case evidenced, can mean nothing but some sort of severe infection. Laparotomy proved that the operation was unnecessary because there was no blood in the peritoneal cavity the subsequent hysterectomy for the purpose of preventing possible further hemorrhage so long after delivery seems hardly justifiable even though the abdomen was opened. Better to have closed the abdomen without further operating on a patient as ill as this one was. Fortunately puerperal infections caused by *Cl. welchii* are extremely uncommon. It is quite a coincidence that two cases infected by this organism should be reported in this column.

ZINC PLATES OF PHYSICIANS

Upon a number of occasions recently the attention of the Committee on Ethics and Discipline has been called to material which has appeared in various local newspapers throughout the state. This material takes the form of a fairly large sized zinc plate showing a physician in a center surrounded by various drawings which illustrate events in his life.

As a rule the newspapers gain no direct profit from publishing the plate, and the physician is led to believe that he is contributing to a worth-while local project. Subsequently he is given an opportunity to purchase the original drawing from the artist.

When a series of these appear it usually results in unpleasant repercussions among local physicians and probably does not add to the dignity of the profession. It has been suggested that all members of the Society be warned against participating in such a scheme.

ALEXANDER S. BEOG, M.D., Secretary

DEATH

THOMPSON—FREDERICK H. THOMPSON M.D., of Fitchburg died December 14. He was in his ninety-fifth year.

Born in New Salem, he attended New Salem Academy and Phillips Exeter Academy. He received his degree from Harvard Medical School in 1870 and served as surgical intern at the Massachusetts General Hospital. Immediately after graduation he became physician at the state industrial school for girls in Lancaster and four years later moved to Fitchburg and started private practice.

Dr. Thompson was a founder of the Fitchburg Hospital in Fitchburg where he was chief surgeon for many years. He also served as medical examiner for several years.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His son, a daughter, three grandchildren and one great-grandchild survive him.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

COGSWELL—LEON H. COGSWELL M.D. practicing physician, civic and political leader and prominent in state military circles died suddenly at his home in Warrenton, November 25 at the age of fifty-nine.

Dr. Cogswell was born December 7, 1879 the son of Dr. John R. and Ellen (Hildreth) Cogswell. He was graduated from the New York University College of Medicine in 1901. After serving his internship in New York City he returned to Warrenton in July, 1901. For a while he worked with his father and later took over the latter's practice carrying it on up to the time of his death.

In August 1918 Dr. Cogswell joined the Medical Corps of the U. S. Army with the rank of captain. He served with the base hospital unit at Camp Hancock in Augusta, Georgia and later at Camp Dix in Wrightstown, New Jersey. In 1923 shortly after the reorganization of the New Hampshire National Guard Dr. Cogswell joined the organization and was assigned to the medical detachment. In 1929 he was promoted to the rank of major and became commanding officer of the 19th Regiment, Coast Artillery, Anti-Aircraft, a position which he held at the time of his death.

Surviving him are his wife, Mrs. Annie U. Cogswell and three sons, Richard U., William N. and Dr. Thomas G. Cogswell all of Warrenton.

HENRY H. ANDERSON, Neurologist

MISCELLANY

VERMONT NEWS

VERMONT DEPARTMENT OF PUBLIC HEALTH

The following communicable diseases were reported to the office of the Department of Public Health during the month of October: chickenpox 141, mumps, 14; diphtheria 1, undulant fever, 1, measles, 65, Vincent's infection, 3, German measles, 9, poliomyelitis, 15, scarlet fever, 22, whooping cough, 138; tuberculosis, 13.

The Laboratory of Hygiene made 2775 examinations, the details of which are

Examinations for diptheria bacilli	76
" typhoid fever (Widal reaction)	80
" undulant fever	149
" gonococci in pus	144
" tubercle bacilli	31
" syphilis	1424
" of water bacteriological	709
water bacteriological and chemical	121
milk bacteriological	159
" milk submitted for chemical only	31
" milk submitted for microscopical only	0
" milk submitted for (for bacteria only)	56
" foods	2
" drugs	2
" for coarct, ectoparasites	62
" miscellaneous	3
Antisepsis & complete death report	0
Parasitology (specimen for typing)	0

Activities for the month for the Division of Communicable Diseases included the taking over of the clinic at the Free Dispensary for the treatment of syphilis, the beginning of the program in the high schools and the organization of the social hygiene program for the freshmen at the University of Vermont. Arrangements have also been completed throughout the state for the "clinic" treatment of indigent cases of gonorrhea or syphilis.

The work of the sanitary engineer during this month required travel over practically the entire state. A majority of the time was spent on water supply problems. These included the annual inspection of railroad passenger-car water supply facilities made for the United States Public Health Service.

The Crippled Children's Division reports 195 visits by nurses. The hospital report shows 15 patients in hospitals at the beginning of the month, 15 admitted during the month and 22 discharged. One hundred and forty-six pieces of apparatus were fitted during the month. The

Occupational Therapy Division reports 31 home visits and sales of \$212.15

The director of the Maternal and Child Health Division attended several conferences and gave several lectures. A conference was also held with the state and territorial health officers in Washington, District of Columbia, with discussion on merit systems. Several of the members of the staff of the Public Health Nursing Division attended the American Public Health Association meeting in Pittsburgh. Six hundred and eighty-six baby booklets, 140 diphtheria consent cards and 452 notifications of birth registration were sent out in October.

MARITAL TUBERCULOSIS

Frequently the physician is asked whether or not it is safe for a tuberculous person to marry. The danger of infecting children who may be born of a tuberculous parent is well recognized. What of the possibility of infecting the other marital partner? Because of contradictory expressions of opinion on this point, H. I. Spector (*Marital Tuberculosis*, *Am. Rev. Tuberc.*, 40:147-156, 1939) sought for an answer by means of the statistical method. An abstract of his paper follows.

Marital tuberculosis is defined as the development of clinical tuberculosis in both husband and wife. One must not, however, apply this definition dogmatically, for it cannot, in all cases, be assumed that the disease has been transmitted by the consort, and it is also possible for a tuberculous consort to marry a supposedly non-tuberculous mate who at the time of marriage had an unrecognized latent or active tuberculosis. But undoubtedly infection from the tuberculous marital partner to the healthy one takes place in the majority of instances of marital tuberculosis.

A review of the literature regarding marital tuberculosis reveals that conclusions of various writers contradict each other. The frequency of marital tuberculosis is reported by one writer as 2.9 per cent, by another as 58 per cent and by several others as variations between these figures. The more recent literature, however, seems to concur with the view that tuberculosis is much commoner than in the general population.

The writer received 208 replies from questionnaires sent to physicians in the United States and European and South American countries. There was a divided opinion as to the frequency of marital tuberculosis in married couples, the majority believing that tuberculosis in both husband and wife is not common. Many, however, believed the incidence to be greater than in the general population. The number of physicians who were inclined to permit marriage between arrested tuberculous individuals was greater than those who permitted marriage of a tuberculous individual with a non-tuberculous one. The majority permitted tuberculous couples to have children, but with reservations.

In addition to these collected opinions the author made a study of marital tuberculosis based on 11,193 cases of tuberculosis reported during a ten-year period to the Health Division of St. Louis. From this group came 210 couples (420 persons) all with clinical, active disease. It was found that while only 3.8 per cent of the reported cases of tuberculosis in married people are in both husband and wife, nevertheless the risk of contracting the disease when in marital contact with an active case is twenty-nine times greater than it is in the general population.

About one third were Negroes—the rest Whites.

Sputum was positive in both consorts in 20 per cent of cases, positive in either wife or husband only in about 25 per cent. In 55 per cent, sputum was negative or questionable.

Interested in knowing whether the danger of infection from the marital tuberculous partner is greater to the healthy consort or to the other contacts, especially children, case histories from the viewpoints of infection and the development of clinical disease in contacts were analyzed. It was found that the incidence rate in contacts was 9 per cent or sixty-nine times greater than in the general population.—Reprinted from *Tuberculosis Abstracts*, December, 1939.

COMMITTEE ON PHARMACOTHERAPY AT HARVARD

Harvard University recently announced the formation of a University Committee on Pharmacotherapy, coordinating the efforts of practicing physicians and Harvard scientists in biology, chemistry and medicine, in order to develop research and improved graduate training in the field of pharmacology and experimental therapeutics.

Funds to support the work of the committee for the next five years have been donated by a group of corporations interested in medical and therapeutic research.

"Recent activities in pharmacology and chemotherapy hold promise of important development in the treatment of disease," said Dean C. Sidney Burwell, of the Harvard Medical School, in announcing the formation of the committee. He added "The adequate exploration of this field necessitates close co-operation of various departments of the University."

Formation of the committee follows the policy of President James B. Conant to lower the customary barriers separating the activities of the different departments of arts and sciences.

Dr. Soma Weiss, Hersey Professor of the Theory and Practice of Physics, Harvard Medical School, is chairman of the committee, the function of which will be to bring together men concerned with diverse aspects of therapeutics, including chemists and biologists from the Harvard Faculty of Arts and Sciences, pharmacologists, physiologists and biochemists from the Harvard Medical School and physicians working with patients in hospitals.

Other committee members are Dr. Fuller Albright, assistant professor of medicine, Dr. Henry K. Beecher, associate in anesthesia, Dr. Burwell, ex officio, Dr. Walter B. Cannon, George Higginson Professor of Physiology, Dr. William B. Castle, professor of medicine, President Conant, ex officio, Dr. Louis F. Fieser, professor of chemistry, Dr. A. Baird Hastings, Hamilton Kuhn Professor of Biological Chemistry, Dr. Frederick L. Hisaw, professor of zoology, Dr. Otto Kroyer, associate professor of comparative pharmacology, and Dr. Reginald P. Linstead, professor of chemistry.

"As a result of the co-operation of investigators in various parts of the University, it is hoped that pharmacology and experimental therapeutics will be more effectively cultivated and that an opportunity will be afforded for a new and improved graduate training in the field of pharmacology and experimental therapeutics," Dr. Burwell said. He added that graduate students entering the study program will find the preparation suitable for a number of fields, including the pharmaceutical industry.

CORRESPONDENCE

PROPOSED NEW PLAN OF DENTAL EDUCATION AT HARVARD

To the Editor During the past year a Harvard University committee has been studying the problems of dental education. The report of this committee has been considered by the Faculty of Medicine and by the administrative authorities of the university.

No official statement regarding the suggestions of the committee has yet been released. Nevertheless various accounts based entirely upon rumor have appeared. It is unfortunate, both for the Harvard Dental School and for dental education, that many irresponsible and misleading statements have been made which in large part are without foundation in fact.

It is not possible at this time to release the details of the plan which has been formulated but it is expected that a full account of it will be made public not later than January 1. In the meantime the following observations may serve to correct some of the many misapprehensions that now exist.

1. Harvard is not "going to end its dental school after seventy years"
2. It is not true that, as of this fall, the Harvard Dental School has ceased to exist. As a matter of fact the Harvard Dental School did accept this fall the usual first year class, with a full quota of students, and will carry this class through the entire four years under the present framework.
3. There is no truth in the statement, as applied to the present situation, or to the contemplated new plan, that "all candidates contemplating the study of dentistry must first enroll and qualify by acquiring the degree of doctor of medicine, before entering upon the study of dentistry."
4. The statement that the objective of the new course in dentistry will be not to train men for the general practice of dentistry is misleading. What ever new plan is adopted, it will still be possible for men to qualify for general dental practice and to satisfy requirements for licensure.
5. The statement that the Harvard Dental School is going to discontinue teaching prosthetic and other forms of restorative dentistry and confine itself simply to preparing men for oral surgery and other specialties is wholly without foundation in fact.
6. The dental profession may rest assured that any modifications in the curriculum now under consideration will, if put into effect, be expected to elevate the importance of dentistry as a profession and neither to lower its standards nor to diminish its effectiveness.
7. Until a full account of the plans of the new course has been presented officially we ask the many who are interested in the Harvard Dental School and in the progress of dental education to delay judgment.

LEROY M. S. MINER, Dean
Harvard Dental School

AGREEMENTS OF MEDICAL AND SURGICAL ASSOCIATES AND HEALTH SERVICE, INCORPORATED

To the Editor Following your request for more detailed information in regard to the medical care and service furnished by Medical and Surgical Associates to the subscribing members of Health Service, Incorporated I enclose herewith copies of four agreements in effect or

proposed that cover various aspects of the scheme. Some of the forms will undoubtedly be subject to change before going into effect. Suggestions and criticisms will be welcomed.

CHANNING FROTHINGHAM, M.D.,
for Medical and Surgical Associates.

PARTNERSHIP AGREEMENT OF MEDICAL AND SURGICAL ASSOCIATES

ARTICLES OF AGREEMENT made this first day of November 1939 by and between Allan M. Butler of Brookline, County of Norfolk and Commonwealth of Massachusetts; Hugh Cabot of Cambridge, County of Middlesex and said Commonwealth; Robert L. DeNormandie of Lincoln, County of Middlesex and said Commonwealth; Channing Frothingham of Boston, County of Suffolk and said Commonwealth; and Edward L. Young of said Brookline.

1. The parties above named hereby agree to associate together as partners under the firm name of Medical and Surgical Associates for the purpose of establishing maintaining and operating a health plan whereby medical care and services may be provided by individuals who are legally qualified to give such medical care and services to such of the public as become subscribers to the plan and make monthly or other regular payments in accordance therewith and for the further purpose of entering into contracts with other organizations which operate similar health plans whereby Medical and Surgical Associates agrees to furnish medical care to members of the health plans of said organizations through themselves or through other physicians associated with them by agreement.

2. Said partnership shall commence on the first day of November 1939 and shall continue for a period of five years from said date and for such further time as the partners may agree upon.

3. The business of the partnership shall be carried on at Boston Massachusetts, and at such other place or places as the partners shall hereafter from time to time determine.

4. Each partner shall devote such of his time to the business of the partnership as appears necessary from time to time and is not incompatible with his other professional obligations.

5. Each partner shall contribute such amounts of capital as shall be mutually agreed upon from time to time.

6. Interest at the rate of four per cent shall be paid on the capital contributed by each partner.

7. The members of the partnership shall be paid only for their services in the capacity of consulting or associated physicians and for time actually spent in the management of the partnership. There shall be no drawing accounts. The profits of the partnership shall not be distributable to the partners. All net profits shall be added to a reserve fund to be established and maintained by the partners which shall be used for the sound and efficient conduct of the business. Any amounts of said fund, or any profits, which shall not be required for said purpose shall be used insofar as the partners shall deem proper to increase the income available to physicians associated or employed in the rendering of medical care by the partnership to improve the standard of medical care rendered by the partnership, or to decrease the cost of said medical care to subscribing members of said health plans. Any losses which shall happen to the said business shall be borne and paid by the said partners equally. Any amounts so paid by the partners in one year may be reimbursed to them from income of subsequent years.

8. There shall be kept at all times during the con-

continuance of the partnership full and correct books of account wherein all of the said partners shall enter all moneys by them or any of them received, paid out or expended in connection with the said business and all other matters and things whatsoever to the said business and the management thereof pertaining, which books shall be used in common between the said partners so that any of them may have access thereto without any interruption or hindrance of the others. All business transactions of the said partnership shall be carried out only with the knowledge and consent of all partners. The moneys belonging to the partnership shall be deposited in some bank mutually agreed upon, and all drafts upon the same shall be made in the name of the partnership.

9 The parties hereto mutually agree to and with each other that during the continuance of their partnership none of them will endorse any note or otherwise become surety for any person or persons whomsoever without the consent in writing of the other parties.

10 On or before the first Monday of February in each year for as long as the partnership shall continue, a general account shall be made and taken by the partners of all receipts, payments, engagements and transactions of the partnership during the then preceding fiscal year, which shall be from January 1 to December 31, and all capital, property, engagements and liabilities for the time being of the partnership, and from this the amount of the net profits for the said preceding year shall be determined, said profits to be used as provided in Paragraph 7 above.

11 The death of any partner shall not dissolve the partnership between the remaining partners. In case of the death or retirement of any partner, the said retiring partner or the estate of the said deceased partner shall be entitled to any amounts of the capital contributed by the said partner. Such retiring partner or such estate of a deceased partner shall not have or be entitled to any other payment or interest.

12 At the termination of the partnership, the partners will make each to the others full and correct accounts of all things relating to their said business, and all the remaining assets of the said partnership shall go to the Boston Medical Library.

IN WITNESS WHEREOF the said parties hereunto set their hands and seals on the day and year first above written.

CHANNING FROTHINGHAM,
EDWARD L. YOUNG,
HUGH CABOT,
ALLAN M. BUTLER,
ROBERT L. DENORMANDIE

PROPOSED AGREEMENT BETWEEN HEALTH SERVICE, INC.,
AND MEDICAL AND SURGICAL ASSOCIATES

THIS AGREEMENT, made this day of 1939, by and between Health Service, Inc., a Massachusetts corporation duly established by law, and Allan M. Butler of Brookline, County of Norfolk and Commonwealth of Massachusetts, Hugh Cabot of Cambridge, County of Middlesex and said Commonwealth, Robert L. DeNormandie of Lincoln, County of Middlesex and said Commonwealth, Channing Frothingham of Boston, County of Suffolk and said Commonwealth, and Edward L. Young, of said Brookline, co-partners doing business under the firm name of Medical and Surgical Associates, WITNESSETH

WHEREAS, Health Service, Inc., is a Massachusetts corporation organized under General Laws, Chapter 180, for the purpose, among others, of establishing, maintaining and operating a non profit health plan whereby medical care and service, both preventive and curative, may be provided at low cost by individuals who are legally qualified to give such medical care and services with whom this corporation shall have contracts directly or indirectly for such care and services to such of the public of low income resident in the said Commonwealth as become subscribers to the plan and make monthly or other regular payments in accordance therewith, and

WHEREAS, Medical and Surgical Associates is a partnership organized for the purpose, among others of entering into contracts with other organizations which operate health plans whereby Medical and Surgical Associates agrees to furnish medical care to the subscribing members of said organizations,

NOW THEREFORE the parties hereto do hereby mutually agree as follows

1 The said Medical and Surgical Associates, through its partners, associated physicians and employees, shall furnish to the subscribing members of Health Service, Inc., who are referred to said Medical and Surgical Associates, all the medical care and services called for by the form of subscribing member agreement hereto attached and hereby incorporated herein.

2 In the furnishing of such medical care, the relation of Medical and Surgical Associates to Health Service, Inc., shall be that of an independent contractor, and Health Service, Inc., its officers and employees shall have no control, authority or power of regulation over said Medical and Surgical Associates, its associated physicians or employees as to the manner, methods or details of the furnishing of said medical care.

3 Medical and Surgical Associates shall designate one of its partners or employees to serve as medical director of the medical services furnished to said members of Health Service, Inc., by Medical and Surgical Associates. The said medical director shall be paid by and subject solely to the authority of Medical and Surgical Associates.

4 Health Service, Inc., shall have the right to inspect all of the business books and accounts of Medical and Surgical Associates pertaining to Health Service, Inc., and its said members at any reasonable time.

5 Medical and Surgical Associates agrees to indemnify Health Service, Inc., against any claims by said members for failure to provide the medical care called for by the subscribing member agreement or for malpractice, and Medical and Surgical Associates agrees to carry the usual policies of insurance against claims of this nature.

6 Health Service, Inc., agrees to pay quarter annually to Medical and Surgical Associates not less than eighty per cent of all payments received from its said members, with the exception of initial registration fees, and as much more than eighty per cent as is compatible with the sound operation of Health Service, Inc., with the exception that a less per cent may be paid during the first year of operation.

7 Medical and Surgical Associates agrees that the members of the partnership shall receive compensation from said payments only for their services in the capacity of consulting or associated physicians and for time actually spent in the management of the partnership, that there shall be no drawing accounts for members

of the partnership that the profits of the partnership shall not be distributable to the partners that all net profits of the partnership shall be added to a reserve fund to be established and maintained by the partners which shall be used for the sound and efficient conduct of the business and that any amounts of said fund, or any profits which shall not be required for said purpose, shall be used insofar as the partners shall deem proper to increase the income available to physicians associated or employed in the rendering of medical care by the partnership to improve the standard of medical care rendered by the partnership or to decrease the cost of said medical care to subscribing members of said health plan and that at the termination of the partnership all the remaining assets of the said partnership shall go to the Boston Medical Library

8 This agreement and the rights and obligations of the parties hereunder shall continue in effect until terminated by either party by notice in writing to the other at least six months prior to the date of termination.

14 WITNESS WHEREOF the parties hereto have set their hands and seals on the day and year first above written.

AGREEMENT BETWEEN HEALTH SERVICE INC., AND SUBSCRIBING MEMBER

Health Service, Inc., agrees with the subscribing member named on the membership card issued in conjunction herewith to make available to said member (and dependents) according to the terms and conditions of the membership card and the provisions hereinafter set forth the benefits of the agreements between Health Service, Inc., and duly licensed and qualified physicians whereby said physicians agree to furnish to members of Health Service, Inc., medical care and services in accordance with the provisions set forth hereunder

Health Service, Inc. (hereinafter referred to as Health Service) is incorporated under the laws of the Commonwealth of Massachusetts as a non-profit organization.

I Medical Care to Be Rendered

A Health Service associated physicians will render to members (and dependents) medical care according to the terms and with the exceptions hereinafter set forth such medical care to consist of examination and the diagnosis of any pathological condition together with the treatment of the same, whether the treatment be by means of physiotherapy, medication, manipulation or application of splints and dressings and all preventive care operations and treatments recognized as standard treatment in the condition under observation by the medical and surgical profession including clinical and laboratory tests, x-ray study and professional consultations. Health Service associated physicians shall render twenty-four hour service by telephone and shall respond to demands for domiciliary care, office care, consultation and treatment. The associated physician shall determine, subject, in case of question by the patient, to the approval of the Health Service medical director, the nature and extent of the medical care required by the patient's condition.

B. When ordered by an associated physician Health Service shall furnish to a patient ambulance service not to exceed fifteen riding miles travel by the patient on any one trip.

II. Exceptions and Exclusions to Care Rendered

A The medical care provided for herein shall not include treatment for mental alcoholic or drug addiction

diseases or illnesses arising out of or induced by intoxication or drug addiction of the patient, or radium and x-ray therapy for tumor or cancer

B All orthopedic appliances, artificial limbs, trusses, glass eyes appliances for deafness, artificial teeth, eye glasses, crutches, wheel chairs, sick-room furniture, nursing care, hospitalization, blood-transfusion donors and medicinal preparations prescribed for and used by or furnished to a patient, for which a charge is made will be paid for by the patient.

C. The cost of medicinal preparations required for hypodermic, intramuscular, intravenous or intraspinal injections and hormone or vitamin therapy shall be borne by the patient but the treatment, except for the cost of said medicinal preparations shall be furnished by Health Service.

D With respect to any condition known to require medical care prior to the date of execution of an application for subscribing membership treatment for the same may be given conditionally upon the payment of special charges to be mutually agreed upon by Health Service and the subscribing member.

E. Health Service will not furnish dental diagnosis or care of any nature or x-rays associated therewith.

F Health Service will assume no responsibility, financial or otherwise, for any medical care given or recommended by a physician not associated with Health Service.

G Health Service shall be subrogated to the rights of the subscribing member (and dependents) in the event of an existing right to recover or recovery from any third party of the cost of medical care furnished by Health Service.

H. The medical care provided for herein shall not include treatment of a patient suffering from any injury arising out of and in the course of the employment of the patient and compensable under the Workmen's Compensation Act of the Commonwealth of Massachusetts, or any similar state or federal law. The member shall be personally responsible for the reasonable value of all services rendered in the treatment of any such injury unless payment therefor shall have been made to Health Service by the employer of the patient or an insurer of said employer or a decision shall have been rendered under the Workmen's Compensation Act determining that the patient's injury did not arise out of and in the course of his employment and is not compensable under the Workmen's Compensation Act.

III Location of Patient

A. To receive domiciliary medical care, the patient must be located within a radius of 3 miles of an associated physician.

B To receive medical care the patient must go to the office of an associated physician designated by Health Service.

C. To receive medical care in a hospital the patient must go to the hospital recommended by an associated physician.

IV Arbitration

The member, by application for and acceptance of this certificate agrees with Health Service that in the event of any controversy between the member and Health Service, Medical and Surgical Associates, or any associated physician said controversy will be settled by arbitration and that for said purpose one arbitrator shall be selected by the member and one arbitrator selected by Health

Service (or Medical and Surgical Associates, or the associated physician), and a third by the two so selected, whereupon the controversy will be submitted to the said three arbitrators, and a decision rendered by a majority thereof shall be final and binding upon the member and Health Service (or Medical and Surgical Associates, or the associated physician)

V Change of Rates or Services

Health Service, upon ninety days' notice to the member either by a notice mailed to his home address as it appears upon the records of Health Service, or delivered to the member's remitting agent as Health Service may elect, may change the subscription rate, the schedule of special charges, or the services to be rendered hereunder. The member shall have the right to terminate this agreement, if the member so desires, upon the effective date of said change by notice in writing to Health Service.

VI Special Charges

A In order to provide for equitable distribution of the costs of medical care furnished under the Health Service plan, the following special charges in addition to the regular membership rate shall be paid to Health Service by the member immediately upon the rendering of the services

Domiciliary calls, each	
Between 7 a.m. and 7 p.m.	\$1 00
Between 7 p.m. and 7 a.m.	\$1 50

Charges for domiciliary calls shall be made only for the first four calls for each individual sickness within a period of any two consecutive months

Obstetrical care, including prenatal and postnatal care, but excluding domiciliary calls, payable in five monthly installments beginning at the fourth month of pregnancy	\$25 00
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In case of early termination of pregnancy a proportionate amount of the \$25 00 will be charged, dependent upon the amount of care received

X-ray service, depending upon extent of study	\$1 00—\$5 00
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B Treatment for excepted conditions, if desired by the member, and treatment of existing illness or disability of persons who do not pass the physical examination, will be rendered by Health Service at special rates mutually agreed upon by the member, or by such person, and Health Service.

C An associated physician will, at the request of and upon the payment of a reasonable charge by the member (or dependent), fill out forms, make reports and give statements and testimony concerning information acquired when attending said member (or dependent) patient.

VII Recommendation Concerning Hospital Service

In order that the most efficient care may be given by Health Service, it is strongly recommended that the member be a subscriber of an associated hospital service or hospital insurance plan, and that such dependents as are covered by this agreement be also entitled to hospital benefits under the associated hospital service or insurance contract.

VIII Termination

This agreement shall be effective until terminated. This

agreement and all rights hereunder may be terminated by either party upon notice to the other party in writing given ninety days prior to the date of termination, and shall be terminated at any time upon default by the member in the payment of charges in accordance with the terms hereof and all benefits to the member and dependents hereunder shall automatically cease after such default.

IX Definitions

The following words as used in this certificate, unless the context otherwise requires, shall have the following meanings

Subscribing Member A person who has signed a form of application with Health Service, and who has been accepted by Health Service as a subscribing member (herein called "member")

Dependent The husband or wife of a member or an individual who is totally dependent upon the member for support, who resides in the same home as the member and who is related to the member by blood or marriage and who is accepted and registered as such by Health Service.

Patient A member or dependent of a member who is in need of medical care.

Associated Physician A physician licensed to practice medicine and surgery in the Commonwealth of Massachusetts and directly or indirectly associated by agreement with and so designated by Health Service

Domiciliary Care The attendance of a patient by an associated physician at any place other than an associated physician's office or recommended hospital.

X Membership Rates

There shall be a registration charge of \$3 00 for each person applying to become a member. There shall be no registration charge for dependents. One dollar shall be payable at the time of registration and the balance shall be payable 50c a month for the succeeding four months. If an applicant for whom an examination is required is rejected, the \$3 00 shall be kept by Health Service as the cost of examination and the report thereon.

Membership rates are as follows

Individual	\$1 50	per month
Individual and husband or wife	\$2 50	" "
For each child under 2 yr. of age	\$1 00	" "
For each child over 2 yr. of age and under 21 yr.	50	" "
Maximum family rate for husband and/or wife and dependents under 21 yr.	\$4 00	" "
For each dependent over 21 yr.	\$1.50	" "

Payable in monthly installments unless otherwise provided.

XI Requirements for Eligibility

The requirements for eligibility to become a member or to be registered as a dependent are as follows

A The member shall be a member of a group accepted by Health Service, shall have an annual income of not more than \$3500 and be a resident of Massachusetts

B Any male over fifty years of age or any male applying more than ninety days after membership is open to members of the group, or any female, shall, before becoming a member, pass a medical examination given by an associated physician of Health Service

C. Health Service will accept or reject dependents or request a medical examination of a dependent on the basis of information given by the member at the time of his application.

XII. Non-Transferable

This agreement and all rights hereunder are non-transferable. Members shall receive medical services only. They shall not be entitled to any payments of cash or any reditu.

XIII Responsibility

Health Service shall not be responsible for acts of negligence or other wrongful acts of associated physicians.

XIV Non-Profit

Health Service is operated for the benefit of the subscribing members. Members shall be entitled to such additional benefits if any as may be determined from time to time by the Board of Directors.

AGREEMENT BETWEEN MEDICAL AND SURGICAL ASSOCIATES AND ASSOCIATED PHYSICIAN

THIS AGREEMENT made this _____ day of _____ 1939 by and between _____, hereinafter called the party of the first part, and Allan M. Butler, Hugh Cabot, Robert L. DeNormandie, Channing Frothingham and Edward L. Young, co-partners doing business under the name of Medical and Surgical Associates, hereinafter called the party of the second part, WITNESSETH

WHEREAS the party of the first part is a physician duly licensed to practice under the laws of the Commonwealth of Massachusetts, and

WHEREAS the party of the second part is a partnership organized for the purpose of establishing maintaining and operating a health plan whereby medical care and services may be provided by individuals who are legally qualified to give such medical care and services to such of the public as become subscribers to the plan and make monthly or other regular payments in accordance therewith and for the further purpose of entering into contracts with other organizations which operate similar health plans whereby Medical and Surgical Associates agrees to furnish medical care to the subscribing members of the health plans of said organizations, and

WHEREAS the party of the second part desires to enter into an agreement with the party of the first part whereby the party of the first part shall assist the party of the second part in the rendering of medical care to subscribing members of the health plan of any organization with which the party of the second part has an agreement for the furnishing of medical care,

NOW THEREFORE the parties hereto do mutually agree as follows:

1 (Clause for general practitioner) The party of the first part agrees to furnish general medical care as provided in the form of Health Service, Inc., subscribing member agreement attached hereto and hereby incorporated herein to such members and dependents of members as shall be referred to the party of the first part by the party of the second part and accepted by the party of the first part.

(Clause for specialist) The party of the first part agrees to furnish medical services in the line of _____ in accordance with the form of Health Service, Inc.,

subscribing member agreement attached hereto and hereby incorporated herein to such members and dependents of members as shall be referred to the party of the first part by the party of the second part and accepted by the party of the first part.

2. The party of the first part agrees to accept payment for all of said services according to the following plan of operation: quarter-annually the medical director of the health plan to be designated by Medical and Surgical Associates, shall obtain from all associated physicians of Medical and Surgical Associates reports of all services rendered by them to members of said health plans and to members dependents, and on the basis of the said reports shall make a report to Medical and Surgical Associates who shall determine the fair proportion of the net income or reserve funds of the partnership to which each associated physician shall be entitled. Payment of said proportionate amounts shall be made quarter-annually.

3. The party of the first part shall incur no expense for or in the name of Medical and Surgical Associates other than as provided in Paragraph 2 above without specific authorization by Medical and Surgical Associates.

4. The party of the first part shall use as consulting physicians in connection with patients referred to the party of the first part by the party of the second part only such physicians as shall be designated or specifically authorized by Medical and Surgical Associates.

5. The party of the first part agrees to abide by rules pertaining to administrative matters promulgated from time to time by Medical and Surgical Associates in connection with patients referred to the party of the first part by the party of the second part.

6. This agreement and the rights and obligations of the parties hereunder shall continue in effect until terminated by either party by notice to the other in writing at least ninety days before the date of termination.

7. The party of the first part agrees to carry a policy of insurance against liability as a physician covering all acts which may be performed by the party of the first part under this agreement, said policy to be for an amount not less than \$5000 for claim by one person and \$10000 for claims by more than one person.

IN WITNESS WHEREOF the said parties hereto set their hand and seals on the day and year first above written.

A TRIBUTE TO GEORGE REYNOLDS

To the Editor Since George Reynolds' death some months ago I have had occasion to see a number of his patients. What was apparent before is even more so now—he was a rare physician, in possessing as he did a perfect combination of human understanding and loving kindness and of scientific knowledge. He is being sorely missed.

I should also like to add a personal tribute to him as a patient himself. Despite the fact that he had been afflicted for years by a severe physical handicap he went ahead uncomplainingly to make of his life a shining example of fortitude, service and happiness.

PAUL D. WHITE, M.D.

Massachusetts General Hospital
Boston.

A REPLY TO DR JOSLIN'S SUGGESTIONS

To the Editor The trustees of Middlesex University are deeply appreciative of the sympathetic interest that Dr Elliott P Joslin has shown in their problems and are indebted to him for his excellent and constructive suggestions for the advancement of the School of Medicine, as published in the November 30 issue of the *Journal*. They would enthusiastically welcome Dr Joslin to membership on the Board of Trustees and are entirely ready and willing to carry out the recommendations which he has enumerated as a condition precedent to his acceptance.

The real burden lies upon the alumni, to whom Dr Joslin has assigned the feat of raising a substantial sum to be applied to specific requirements of the School of Medicine. The trustees very sincerely hope that the alumni may find themselves equal to this task and may be able to do their share toward the end that the School of Medicine shall attain a fully accredited position in the field of medical education.

C RUGGLES SMITH, *President*,
Middlesex University

Waltham, Massachusetts

ANENT SOCIALIZED MEDICINE

To the Editor On November 7 I had the rare opportunity of listening to the most forceful speaker and the most brilliant mind I have ever heard. It is indeed a credit to the American Medical Association to have Dr Fishbein as the editor of its journal. In his discussion he gave a most cogent outline showing how mistaken is our government in trying to interfere with the medical profession. He proved conclusively that millions of dollars are wasted in building hospitals and institutions for which neither the medical profession nor the people have any use. He further stated that the medical profession is giving service gratis to millions of people and the cost of that service in his opinion amounts to \$365,000,000 per year or almost twice as much as the government is spending for the same purpose.

He also told us that many clinics now springing up in different parts of the country are a complete failure. But he neglected to tell us why they are a failure, and to tell us why in the last ten years the income of the average physician here is dwindling to almost nothing. Most of the physicians in America are not able to meet their expenses. I am sure that a large majority of the physicians who listened to Dr Fishbein's speech are actually worried when the first of the month comes around. And most of us have to worry about the next day's expenses. In other words, we live from hand to mouth. I can understand why Dr Fishbein talked as he did. A man of his type, although he travels extensively, meets the members of the medical profession who are in the upper brackets and who are economically secure. Most of them practice medicine not to derive a living from it but for the sake of science or tradition or pleasure, and these men have no reason to believe that most physicians are in financial straits. These physicians differ from those in the lower brackets who rely only on the incomes from their practice to support their families and themselves. Ten years ago the people did not flock to hospitals, outpatient departments and free clinics as they do today. Ten years ago there were not so many doctors as there are today, and therefore the question of socialized medicine did not have to be raised. Conditions were not so acute. How could a clinic, no matter how reasonable its charges, compete with clinics which did not charge at all? I would be the last to blame people for

going to free clinics. They get just as good care there with all the latest diagnostic technics and instruments under the supervision of capable men. And if necessary they get consultations with some of the biggest men in that particular locality. Why should they go to private clinics and pay for the same kind of service that they can get free of charge? The individual physician certainly cannot compete with the free clinics. He cannot give the patients as good service as they can get in the free clinics, because generally not only does he not possess the different instruments of precision that have been developed of late but also he does not have the technic of using them. If one were fortunate enough to be able to outfit his office with an x-ray machine, an electrocardiograph, a metabolism apparatus and a complete laboratory, he would have to hire technicians to do all the work. Naturally the patient would have to pay for this. But for no money at all he can go to any of the free clinics in the city and have all that work done under the careful supervision of trained technicians, with correct interpretations of the findings. Very often a physician is forced to treat free of charge, patients in a hospital clinic who formerly were his private patients.

In my opinion, most of these people who now attend clinics will never return to private practitioners, just as the ten or twelve million people out of work now will, it is said, never return to employment in private enterprise. If anything, outpatient departments are definitely increasing. On the other hand the medical schools are certainly not lacking students, and there is no diminution in the number of graduates. So if one is to apply the law of supply and demand, there is certainly an oversupply of physicians in proportion to the number of patients who demand private treatment. My suggestions therefore would be the following:

- 1 Limit the number of graduates to the actual demand.
- 2 Decentralize them, that is, send them from the overcrowded city to other districts or parts of the United States where there is a shortage of physicians, some kind of subsidization, by the government or by the particular place that finds itself without medical care, could accomplish this.
- 3 In the large cities enlarge the outpatient departments so as to facilitate the handling of more patients, and increase the medical staffs and laboratories to double or triple the size they are at present.
- 4 Have the city or state pay all physicians who are eligible and willing to work a certain time of the year at a hospital, the pay to be lucrative enough to attract the best men.
- 5 Put physicians so employed by the city or state through some medical and disciplinary training—one month each year with pay, this would help many physicians to adapt themselves to that particular locality and help specialize them further.

Of course, I know that some will protest to this on the ground that it is the beginning of socialized medicine. My answer is that, since we cannot go against the inevitable, it is healthier to accept it with good grace. If the medical profession will not try to solve its own problem, the politicians will surely get hold, and this will be unfortunate for the profession.

AARON FELDMAN, MD

485 Commonwealth Avenue,
Boston

NOTICES

ANNOUNCEMENTS

DAVID WEINTRAUB, M.D., announces the opening of an office at 520 Beacon Street, Boston.

MAYER HYMAN, M.D. announces the opening of an office at 520 Beacon Street, Boston.

BOSTON DOCTORS
SYMPHONY ORCHESTRA

The Boston Doctors Symphony Orchestra will rehearse under Alexander Theide, former concertmaster with the Cleveland Symphony Orchestra and the Philadelphia Symphony Orchestra every

Thursday at 8:30 p.m., in Studio A Station WMEX 70 Brookline Avenue, Boston. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel Brookline (BEA 2430)

WALTHAM MEDICAL MEETING

The Metropolitan State Hospital announces that the regular monthly clinicopathological conference scheduled to be held on December 27 will be held on Wednesday evening, January 3 at 8:00 A case showing atypical mental symptoms following trauma and complicated by pulmonary tuberculosis will be presented by Drs. Emerick Friedman and Richard C. Wadsworth. The discussion will be led by Dr. Harry C. Solomon.

All interested physicians are cordially invited.

CONSULTATION CLINICS FOR CRIPPLED
CHILDREN IN MASSACHUSETTS UNDER
THE PROVISIONS OF THE SOCIAL
SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Haverhill	January 3	William T. Green
Lowell	January 5	Albert H. Brewster
Salem	January 8	Harold C. Bean
Gardner	January 9	Mark H. Rogers
Brookton	January 11	George W. Van Gorder
Pittsfield	January 15	Francis A. Slowick
Northampton	January 17	Garry deN. Hough, Jr.
Worcester	January 19	John W. O'Meara
Fall River	January 22	Eugene A. McCarthy
Hyannis	January 23	Paul L. Norton

MASSACHUSETTS DEPARTMENT OF CIVIL
SERVICE AND REGISTRATION

SCHOOL PHYSICIAN SCHOOL DEPARTMENT WATERTOWN

Director of State Civil Service, Ulysses J. Lupien, has recently announced that a competitive examination is to be held on January 17 in order to find eligibles for appointment to the position of School Physician School Department Watertown. The salary is \$500 a year payable in twenty equal instalments of \$25 each. The duties are as follows: to visit daily at least one school house; to visit every school building in said district at least once a week to respond to every emergency call of the principal of each school in said district to make a careful examination of each pupil once a year and new children entering the schools to examine every child returning to

school after an absence for illness from an unknown cause, and unable to get a certificate from the Board of Health because of not having had an attending physician to submit a written monthly report to the Superintendent of Schools and to attend one third of the football games.

The entrance requirements are as follows: applicants must be registered physicians under the State Board of Registration in Medicine.

The subjects and weights are as follows: training and experience 2 practical questions 3 total 5 Applicants must obtain at least 70 per cent in each subject of the examination in order to become eligible. Physical fitness is to be determined by physical examination.

The last date for filing applications is Wednesday January 3 at 5:00 p.m.

MISSISSIPPI VALLEY MEDICAL SOCIETY
1940 ESSAY AWARD

The Mississippi Valley Medical Society offers a cash prize of \$100 a gold medal and a certificate of award for the best unpublished essay on a subject of interest and practical value to the general practitioner of medicine. Certificates of merit may also be granted to the physicians whose essays are rated second and third best. Entrants must be members of the American Medical Association. The winner will be invited to present his contribution before the next annual meeting of the Mississippi Valley Medical Society at Rock Island, Illinois, September 25-26 and 27 1940 the Society reserving the exclusive right to publish the essay in its official publication—the *Mississippi Valley Medical Journal*. All contributions must not exceed 5000 words be typewritten in English in manuscript form, be submitted in five copies, and be received not later than May 1 1940. Further details can be secured from Harold Swanberg, M.D., secretary Mississippi Valley Medical Society 209-224 W. C. U. Building Quincy Illinois.

UNITED STATES MARINE HOSPITAL

The staff meeting of the United States Marine Hospital Chelsea Massachusetts will be held at "The Hut, on Friday January 5 1940 at 4:00 p.m. Dr. Arthur W. Kimpton will talk on the subject "Cardiospasm"

JOHN W. TRASK, Medical Director in Charge

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING
MONDAY DECEMBER 25

TUESDAY DECEMBER 26
10 a.m.—12:30 p.m. Boston Dispensary tumor clinic

WEDNESDAY DECEMBER 27
12 m. Clinicopathological conference Children Hospital amphitheater

THURSDAY DECEMBER 28
10 a.m.—12:30 p.m. Boston Dispensary tumor clinic

*Open to all medical professions

DECEMBER 22—W. Latham Medical Club. Page 150 issue of November 27
DECEMBER 29 ad 30—Phi Delta Epsilon. Page 918 issue of December 7
JUNE 3—Metropolitan State Hospital. Chikara bol g 1 conference
NOTE: born
JUNE 5—U. S. Naval Medical Hospital. Not also
JUNE 16, 18—U. S. Naval Medical Hospital. Not also
JUNE 17, 18—U. S. Naval Medical Hospital. Not also
JUNE 17, 18—U. S. Naval Medical Hospital. Not also

U. S. Naval Medical Library

JANUARY 11 — Pentucket Association of Physicians 8.30 p.m. Hotel Bartlett Haverhill
 JANUARY 22-25 — American Academy of Orthopaedic Surgeons. Hotel Statler Boston
 FEBRUARY 11-14 — International College of Surgeons. Page 759 issue of November 9
 FEBRUARY 22-24 — American Orthopsychiatric Association Page 957
 MARCH 2 JUNE 8 and 10 — American Board of Ophthalmology Page 719 issue of November 2
 MARCH 7-9 — The New England Hospital Association Hotel Statler Boston
 MAY 14 — Pharmacopoeial Convention Page 894 issue of May 25
 JUNE 7-9 — American Board of Obstetrics and Gynecology Page 1019 issue of June 15

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 3 — Semi-annual meeting. Combined meeting with Essex South Danvers State Hospital Hathorne 7 p.m.

ESSEX SOUTH

JANUARY 3 — Head Injuries Dr John S. Hodgson Danvers State Hospital Hathorne

FEBRUARY 14 — Cough Sputum Hemoptysis — How shall they be investigated? Dr Reeve H. Betts Essex Sanatorium Middleton

MARCH 6 — Experimental and Clinical Considerations of Sulfanilamide Treatment of Hemolytic Streptococcal Infections Dr Champ Lyons Lynn Hospital Lynn

APRIL 3 — Addison Gilbert Hospital Gloucester

MAY 8 — Annual meeting Salem Country Club Peabody

HAMPSHIRE

JANUARY 10

MARCH 13

MAY 8

All meetings are held at 11.30 a.m. at the Cooley Dickinson Hospital, Northampton

MIDDLESEX EAST

JANUARY 10

MARCH 20

MAY 15

Meetings are held at 12.15 p.m. at the Unicorn Country Club, Stoocham

MIDDLESEX NORTH

JANUARY 31

APRIL 24

JULY 31

OCTOBER 30

NORFOLK SOUTH

JANUARY 4

FEBRUARY 1

MARCH 7

APRIL 4

MAY 2

All meetings with the exception of one which is usually held at the Quincy City Hospital are held at the Norfolk County Hospital in South Braintree at 12 o'clock noon

PLYMOUTH

JANUARY 18 — Brockton Hospital Brockton

MARCH 21 — Goddard Hospital Brockton

APRIL 18 — State Farm

MAY 16 — Lakeville Sanatorium Lakeville

SUFFOLK

JANUARY 31 — Scientific meeting Subject to be announced later

MARCH 27 — Scientific meeting Symposium on Ulcerative Colitis and Diarrheas Under the direction of Dr Chester M. Jones

APRIL 24 — Annual meeting in conjunction with the Boston Medical Library Election of officers Program and speakers to be announced later

WORCESTER

JANUARY 10 — Worcester City Hospital

FEBRUARY 14 — Worcester State Hospital

MARCH 13 — Worcester Memorial Hospital

APRIL 10 — Worcester Hahnemann Hospital

MAY 8 — Worcester Country Club

Each meeting begins with a dinner at 6.30 p.m. and is followed by a business and scientific meeting

BOOK REVIEWS

Medical Climatology Climatic and weather influences in health and disease Clarence A. Mills 296 pp
 Springfield, Illinois, and Baltimore Charles C Thomas, 1939 \$4.50

As is well known, Dr Mills has for several years been studying the importance to man of climatic environment. Individual articles of his on this broad subject have always been interesting and often stimulating. Now he has put many of them together, added to them, rounded them out, and assembled them in book form. The result is admirable.

It is curious how little serious attention most doctors pay to the effect of climate on disease, how little is taught of this subject in our medical schools, how haphazardly most of us prescribe change of climate to our patients. Yet medical climatology is a serious subject about which a good deal is known. As Dr Mills says, weather and climate together appear to exert a tremendous influence on human welfare. Their effects penetrate deeply into the basic physiologic reactions of the body, altering combustion rate, energy level, rate of growth and development, resistance to infection and many other vital characteristics.

There are eighteen chapters to the volume. These deal with various aspects of medical climatology, for instance, the relation of climate to disturbances of metabolism, to infections, to heart failure and even to suicide and homicide. Each contains interesting information and suggestive ideas. In discussing appendicitis, for example, Dr Mills argues that the patient who develops an acute attack in hot weather carries an additional hazard and should be protected against the deleterious effect of heat. He predicts air conditioning as a matter of course for the modern hospital.

At the end of the book is a list of references to medical climatology. This appears to have been most carefully edited. There is also a useful index. On the whole, Dr Mills is to be congratulated. He has written an interesting book which can be read with pleasure by students, teachers, nurses, hospital administrators and men in general practice.

Le Temps de Réaction Techniques applications cliniques
 Paul Michon. 98 pp Paris Masson et Cie, 1939
 22 Fr. fr

This small book is a brief yet fairly comprehensive review of possibilities in the field of reaction time measurement, principally simple reactions, with a good deal of attention paid to a special technique of reaction to a vibrating stimulus (cessation thereof). Chief interest attaches to the observations with various neurologic conditions. There is a considerable bibliography, from which, however, a number of important early studies are omitted, Cattell's, for example. In this country there has for many years been comparatively little interest in such observations, perhaps because more convenient procedures, using chain reaction principles and language symbols, seemed to yield data of at least equal clinical significance. A distrust of the reliability of these measures made under ordinary clinical conditions has doubtless also played a role in their relative neglect. It may be that the differentials here reported are large enough to outweigh this consideration. If so it should be well worth while to design a bedside instrument of this type, utilizing a synchronous motor and one more compact than those illustrated in the present work.

The New England Journal of Medicine

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VOLUME 221

DECEMBER 28, 1939

NUMBER 26

EMPHYEMA IN CHILDREN*

THOMAS H. LANDEAN, M.D.,† AND HENRY L. HEYL, M.D.‡

BOSTON

THE successful treatment of acute empyema thoracis depends on so many variable factors that it is extremely difficult to evaluate the results in any single series. For the same reason the comparison of series of cases treated by different men at different institutions is also difficult. More accurate conclusions may be drawn from the analysis of the results obtained from an individual institution. Especially is this true if the number of cases is adequate, the direction of treatment is to all intents and purposes in the same hands and each period covers a number of years.

This report presents a further analysis of the cases of empyema operated on at the Children's Hospital in Boston. Three previous reports from this hospital (Ladd and Cutler¹ and Hudson²) go through the year 1928. From January, 1929 through December, 1938, there were 287 additional cases. This brings the total to 463 cases but it is with the recent group of cases that this paper is primarily concerned.

Statistically the recent series shows nothing striking as regards the incidence of sex or of the involvement of one thoracic cavity over the other. Boys comprised 59 per cent of the patients, and girls 41 per cent. The left side was involved in 58 per cent of the cases, the right side in 40 per cent and both sides in 2 per cent.

ETIOLOGY

The predominating etiologic organisms and the mortality to each group are shown in Table 1. As was to be expected, the pneumococcus was the invading organism in the great majority of cases—80 per cent. *Staphylococcus aureus* and *Streptococcus hemolyticus* were each responsible for about 10 per cent of the total cases, with the streptococcus showing the highest mortality of the three

groups—33 per cent. Other organisms were found predominant in 0.6 per cent of the series.

MORTALITY BY AGE GROUPS

It is well recognized and has been pointed out by many authors that the mortality in empyema is exceedingly high in children of two years of age

TABLE 1. Relation of Predominant Organism to Mortality

PATHOGENIC ORGANISM	ALL CASES		MORTALITY	
	%	No.	%	No.
<i>Pneumococcus</i>	80.0	373	2.9	10
<i>Streptococcus hemolyticus</i>	10.4	48	33.0	16
<i>St. pharyngealis (group)</i>	9.0	42	11.0	5
Other organisms	0.6	3		

or under. As will be noted in Table 2, the mortality in this age group was about the same in the first and second five year periods—35 and 33 per cent, respectively. There was a decrease to 21 per cent in the third five year period and a very gratifying drop to 4 per cent in the last. The

TABLE 2. Results of Treatment of Empyema in Children (1919-1939)

FIVE YEAR PERIOD	ALL CASES			FIFTEEN TWO YEARS OR UNDER		
	NO. OF CASES	NO. OF DEATHS	MORTALITY %	NO. OF CASES	NO. OF DEATHS	MORTALITY %
1919-1924	94	13	14	20	7	35
1924-1929	86	11	13	21	7	33
1929-1934	150	20	13	57	12	21
1934-1939	137	3	2	46	2	4

mortality for all ages remained at about 13 per cent for the first three of the five year groups but showed a very gratifying drop to 2 per cent in the last.

It is admitted that the drop in the mortality in the last five year period may have been influenced by the virulence of the infecting organisms during that period, but in large part it was due to more efficient handling of individual cases. Although mortality varies from year to year according to the virulence of the organisms in any given year, it also depends to a considerable de-

*Read at the annual meeting of the New England Surgical Society, September 29, 1939.

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gree on the form of treatment applied. If treatment is based not on the indications of the given case and on the infecting organism but on a routine that may have given success in a previous year, the results may be disastrous.

The controversy that has raged off and on since the World War over the relative merits of repeated aspirations, closed drainage and open drainage is the result of the tendency to fit a routine treatment to the patient rather than to modify the treatment according to the individual requirements of the patient. While it is possible that in the next five-year period at our hospital the mortality will rise, it is believed that comparisons of five-year periods each covering a large number of cases are sufficient to minimize the errors which would result from analyzing smaller series taken year by year. In the last five-year period of the series here covered, 1 death occurred in 1935 and 2 in 1934. In 1936, 1937 and 1938 there were 84 cases of all ages but no deaths. This does not include cases undiagnosed before autopsy, or those in which death was due to some other acute primary disease.

FORMS OF TREATMENT

There are three recognized forms of treatment: aspiration, intercostal closed drainage and open thoracotomy, with or without rib resection. It is of fundamental importance to realize that each of these has its sphere of usefulness, its limitations and its contraindications, and that stubbornly to advocate or adhere to any one of them for all cases is to invite disaster.

Aspiration

There is one form of treatment of empyema which is applicable at least in part to all cases, namely aspiration. Its high practical value, regardless of the form of drainage that may be selected, lies in furnishing knowledge of the invading organism, and it should therefore be used in all cases at the start of treatment. In addition to supplying valuable laboratory data, it is of decided advantage in that it relieves mechanical embarrassment due to the accumulation of fluid in the pleural cavity with a minimum of handling and manipulation, especially during the syn-pneumonic stage. With proper infiltration of the skin by novocain, aspiration can be accomplished with a minimum of discomfort and without moving the patient from bed. In very sick patients in the syn-pneumonic stage, whether the responsible organism be the streptococcus, the staphylococcus or the pneumococcus, it is essential to understand that the accumulation of fluid in the pleural cavity is only one manifestation of

the disease. Unless the fluid is sufficient to cause mechanical embarrassment of the heart or lungs its presence is of relatively slight significance to the welfare of the patient. Therefore measures for its removal should never be undertaken by such means as will throw an undue added strain on a patient already critically ill. By the same token at this stage the fluid, whatever the responsible organism may be, is still thin enough to permit its easy removal by aspiration, if removal in a quantity greater than that needed for diagnosis be indicated.

It will perhaps be pertinent to compare acute empyema during the syn-pneumonic stage with acute osteomyelitis. The latter disease in children under two years of age at this hospital twenty-five years ago showed a distressingly high mortality—about 50 per cent. Its mortality in this age group is now between 5 and 10 per cent, very largely because it has been recognized that the lesion in the bone is but one manifestation of a severe and generalized infection. The sick child who has pneumonia and, in addition, fluid in the pleural cavity is now treated as a whole rather than with attention and efforts unwisely focused on the drainage of the fluid. And, as in acute osteomyelitis, when drainage is undertaken it is accomplished by means that give the minimum of trauma and manipulation, even though good "surgical drainage" may not at that time be established.

Intercostal Closed Drainage

Intercostal closed drainage is particularly to be advised in cases where the reaccumulation of fluid after aspiration is so rapid that even daily aspiration fails to give adequate relief. It provides continuous drainage, does away with the discomfort of repeated aspirations and can be accomplished satisfactorily without moving the patient from bed. In many cases, especially those in which the infection is due to the streptococcus, it results in cure. The technic of instituting this form of drainage does not matter to any significant degree provided certain principles are observed. The wound must be small enough for the drainage tube to fit snugly, the usual precautions against allowing air to enter the thorax must be observed, the tube must not be inserted too far within the chest. We have had success with comparatively simple forms of apparatus. In performing the thoracotomy we use a trocar and cannula. A soft-rubber catheter is inserted through the cannula after the trocar has been withdrawn. After removal of the fluid—and this should not be done too rapidly—the catheter is connected with another section of rubber tube, the distal end of which is

placed under water in a container at a lower level than that of the patient's body

In spite of many claims to the contrary, it is our belief that there is no form of closed drainage that stays absolutely airtight for more than a week or two. Also, the necessity for airtight drainage for a longer period than two or three weeks is seldom if ever sufficiently important to be of any consequence. Some years ago an attempt was made for two years to determine the relative value of closed drainage with and without tidal irrigation. The advantages of tidal irrigation are several, but to administer it successfully requires the almost constant attendance of a highly trained and unchanging personnel. Under conditions as nearly optimum as could be obtained the results of these two kinds of closed drainage, as used in alternate cases during the two-year period, showed no appreciable difference either in the length of time spent in the hospital or in the lessening of complications. Tidal irrigation has therefore been abandoned, since its technical disadvantages appear to outweigh any slight advantages that it may possess. The simpler the form of apparatus the better. So far as irrigation is concerned attention is directed to preventing the tube from becoming clogged. If after a week or two particularly in pneumococcal infections, the intercostal tube is not providing adequate drainage, the condition of the patient should by that time be sufficiently improved to warrant open surgical drainage.

The value of intercostal closed drainage is particularly great in early cases and in young patients. Much of the condemnation of drainage by rib resection has been wrongly attributed to the operation rather than to the choice of case in which it is used. Primary open operation, with or without rib resection should seldom if ever be employed for patients under two years of age and should never be employed during the syn-pneumonic stage, regardless of age. This fact is well recognized, but we wish also to emphasize that in many cases long-continued attempts to obtain adequate drainage by closed methods should be abandoned and open drainage substituted. Enough patients have come to the Children's Hospital with chronic emphyema after weeks and even months of inadequate drainage of the pleural cavity by intercostal tube to make us believe that such drainage should not be prolonged much over two or three weeks unless there is obvious evidence of improvement as shown by clinical condition, decrease in the size of the cavity and re-expansion of the involved lung. The patient whose general condition has not improved sufficiently to warrant open drainage after

two or three weeks of closed drainage is a rarity, and in such cases there is usually some other complicating factor, frequently a bronchopleural fistula.

Open Drainage

In properly selected cases, open drainage is one of the most efficient methods available for the treatment of emphyema. As shown by Table 3,

TABLE 3 Efficiency of Surgical Treatment in 243 Recored Cases of Emphyema

TYPE OF TREATMENT	NO OF CASES	AVERAGE PERIOD OF POSTOPERATIVE RECOVERY
Rib resection	168	24
Intercostal drainage	39	40
Intercostal drainage followed by rib resection	36	37

primary rib resection was used in this series in 168 cases out of 243. These were uncomplicated cases which ended in complete recovery. The average hospital stay after drainage had been instituted was twenty-four days, in comparison with forty days for the cases receiving intercostal drainage, and fifty-seven days for those receiving intercostal drainage followed by rib resection. We cannot agree with the opinion that rib resection is an improper form of treatment. Judging from our experience, its chief danger is the unwise selection of cases for its use, particularly as regards the stage of the disease when drainage is to be instituted. In the last five years there has been only 1 death—in a boy of five—where primary rib resection was done. In this case death occurred suddenly thirty-five days postoperatively from what was supposed to have been an embolus although no postmortem was obtained. In any event it is hardly fair to attribute the death to the fact that rib resection had been done thirty-five days previously. There was one other death following primary rib resection in the last five-year period. This patient was less than a year old and we believe that the choice of drainage was an error of judgment although the infant had recovered from the pneumonia and was apparently in excellent shape, and the pus was of the thick pneumococcal type. In the last two five-year periods there were 3 deaths following primary rib resection in children two years of age or younger. These might have been avoided had the less radical method of intercostal drainage been adopted as a preliminary step. It is probable that overconfidence in rib resection had resulted from our success with it. Good as these results were, they might have been even better had we adopted our rule of today of doing no primary

rib resections in patients under two or three years of age

Rib resection is always preceded by a diagnostic tap in order to determine the organism. The ideal case for primary rib resection is that of a child at least two years old, preferably over three, in a fairly good state of nutrition, who has recovered from pneumonia at least a week previously. Particularly if the responsible organism is the pneumococcus and the fluid is thick and full of fibrin will this method be most effective. In such a case the mediastinum is well fixed, the child is not toxic and the open operation permits the operator to free the lung, and in many cases to remove at that time the large masses of fibrin. A double-flanged rubber empyema button is used, and we rely on the respiratory movements of the freed lung to promote free drainage and obliteration of the cavity. There are only rare cases in which irrigation of the cavity is desirable. The child is not acutely ill and he is encouraged to sit up in bed and be active, and after a few days to be up and around the ward. The use of blow bottles or some similar apparatus to promote expansion of the lung is advocated. The empyema button is seldom left in place for more than fourteen days. The clinical condition of the child and the appearance of the cavity under x-ray are the most reliable guides for prognosis during convalescence.

It is appreciated that many of our patients who received primary rib resections were referred to the hospital when they were well over their pneumonia. For this reason, such a large percentage of primary rib resections would not, and probably should not, be found in a series of cases in private practice. Paradoxically, however, this large group of patients, who had a primary rib resection and whose hospital stay was materially shorter than that of the patients receiving intercostal drainage, with or without rib resection, may have received better treatment of their empyema than patients observed from the start of their pneumonia. In other words, because of failure of early diagnosis of the fluid in the chest the necessity for surgery was realized at more nearly an optimum time than is often true of patients in a better economic status. The typical history in these cases was that the child had had a "cold," with cough, high fever and pain in the chest. Pneumonia may or may not have been diagnosed, and the child was kept in bed for a week or ten days. Later the fever recurred and the child was referred to the hospital for possible empyema. Often only one or two visits had been made by a physician. This sort of medical attention is of course not advocated, but the facts here stated

deserve at least close consideration, and certainly confirm our opinion that the surgical drainage of acute empyema is seldom if ever a surgical emergency.

SITE OF DRAINAGE

The best place for incision depends of course on the location of the pus. Drainage of the pus-filled cavity in its most dependent portion is desirable, but it must be borne in mind that if the incision is made too low the diaphragm will tend to rise against the drainage tube as the cavity becomes emptied. This is of particular importance in cases that are receiving intercostal drainage and in which open drainage may be required later. It is seldom desirable to resect a rib lower than the eighth, and the seventh is usually preferable. In the great majority of cases the posterior axillary line is the best. If the intercostal drainage has been done in the eighth interspace, it may be found at the time of rib resection that the removal of the eighth or ninth rib will give inadequate drainage since the diaphragm has ascended to that level. We have had the experience on one occasion of going through the diaphragm under these conditions. While no harm was done, it was at least humiliating.

CAUSE OF DEATH

The occurrence of operative deaths and those following shortly after surgical drainage should make one consider carefully whether or not the surgical procedure was more radical than the case justified. There must, however, be many cases in which the patient dies not because of the empyema but with empyema. Although such cases are included in this series, it is perhaps unfair to attribute a death to empyema when this forms only part of the evidence of a systemic infection. A patient who has had pneumonia, empyema, purulent pericarditis, mastoiditis and a positive blood culture for *Streptococcus hemolyticus* dies of the general septicemia and not of any one manifestation of the infection.

ANESTHESIA

Aspiration, whether exploratory or for drainage, can be accomplished easily under novocain infiltration, and should be. Local anesthesia is feasible in most cases that require intercostal closed drainage, although at times a supplementary, light, nitrous oxide and oxygen anesthesia is helpful and is seldom contraindicated. In the occasional case where a brief general anesthesia is needed for a sick patient, cyclopropane is a valuable anesthetic agent. For open thoracotomy, especially in cases requiring rib resection, a general anesthetic is preferable. If the patient is not in suit-

ble condition to withstand a general anesthetic, these more radical forms of drainage should not be used. For rib resection, nitrous oxide and oxygen is as a rule the anesthetic of choice.

Scoliosis

Our experience with rib resection as well as with intercostal drainage leads to the firm belief that permanent structural scoliosis will seldom if ever result if the empyema cavity has been properly drained, thereby resulting in its obliteration and in complete re-expansion of the lung on the affected side. It is recognized that postoperative x-ray films taken during convalescence when the cavity has not yet been obliterated may show some degree of scoliosis. Our results, however, confirm the impression that endeavors should be made at this time to favor drainage and re-expansion of the lung. If the child is permitted to be as active as his condition warrants, this will aid and hasten re-expansion of the lung and obliteration of the cavity. The scoliosis will then disappear. Therefore active methods advocated for the treatment of scoliosis at this time are contraindicated. If the child is placed on a Bradford frame or some other form of apparatus in order to correct the apparent scoliosis, the immobilization hinders and may even defeat Nature's usually successful efforts to overcome what is only a functional and not a true structural scoliosis.

CHRONIC EMPYEMA

It is beyond the scope of this paper to deal with chronic empyema, but it is pertinent to point out that the best preventive of the condition is adequate treatment during the acute stages of the disease. The incidence of chronic empyema in cases under observation from the start in our hospital is becoming as gratifyingly small as is the mortality in the acute cases.

CHEMICAL THERAPY

The use of sulfanilamide and sulfapyridine can receive only a few words here. While a few patients with streptococcal pneumonia and empyema received sulfanilamide during 1938 the number is too small to permit any reliable conclusions as to the efficiency of the drug in preventing or treating empyema. Sulfapyridine was not given in any of the cases here considered but during 1939 a few patients received it. Admitting the value of the drug in acute pneumonia it is proper to sound a note of caution against continuing its use when the complication of empyema has arisen. No definite statement can be made, but we are under the distinct impression that the pleural exudate in some of the few cases of empyema which have developed during treatment with sulfapyridine has

been more difficult to drain. It has been of a thick, tenacious character, with very little fluid present, and a rather wide exposure, with thorough freeing of the lung was necessary. The patients as a rule were slow in recovering, but time alone will assign the true value to the use of this drug.

SUMMARY AND CONCLUSIONS

An analysis of the treatment of empyema thoracis during the last twenty years is presented. Comparison of mortality statistics of four five year periods shows a gratifying drop in mortality, not only in older children but also in infants. The following conclusions seem justified, though it is realized that many of them have previously been made not only by those in our hospital but by others.

Acute empyema should never be regarded as a surgical emergency.

Children especially those two years of age and under, die with empyema and not because of it.

Empyema must be treated as a complication of a general systemic infection.

The child as a whole must be treated, not merely the condition in the pleural cavity.

The recent improvements in preoperative and postoperative care, particularly from the point of view of fluid balance, are of great importance.

Diagnostic thoracentesis should be done in all cases in order to determine the organism.

The type of drainage instituted must be based on the needs of the individual case. The simpler the form of apparatus used the better.

Primary open drainage, with or without rib resection, should never be done during the syn-pneumonic stage or in children under two years of age. If the patient's condition contraindicates a general anesthetic, methods of drainage requiring a general anesthetic are also contraindicated.

In properly selected cases, primary rib resection is a safe and most efficient method of treatment.

Local anesthesia for aspiration and intercostal closed drainage, and nitrous oxide and oxygen for open drainage, are favored.

Scoliosis need not be feared if the empyema is well drained and the cavity is obliterated by the expanded lung.

The treatment of empyema requires the closest co-operation between the surgeon, the internist and the roentgenologist.

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DISCUSSION

DR ALLEN G RICE, Springfield, Massachusetts Those of us who recall the treatment of empyema in the days of the World War realize the lessons that we have learned since then. These have evidently stuck, and all that remains for me to do is to emphasize certain points which were brought out by Dr Lanman.

In the first place, the presence of empyema does not constitute an emergency, in the second place, one must not be in a hurry to operate on those who have it. My former chief in the Boston City Hospital, Dr Gavin, was always urging us not to operate on cases of empyema until they were "ripe," by which he meant until there was thick pus. In the meantime, he advised continued aspiration.

The third point, which seems to me equally important, is that the surgical procedure should fit the patient. No one operation will cure all such cases, and proper selection and conduct of the operation have more to do with the eventual outcome than any other factors.

Aspiration, it seems to me, is the first thing to be done, and it should be repeated. Rib resection is to be considered a last resort, especially in children.

Recently a young surgeon came to Springfield who is specially trained in chest work, and the tendency is to turn over all such cases to him. So far this practice has proved worth while, and we have every reason to believe that what little mortality exists will decrease in this surgeon's hands. I believe that these cases can be handled much better by one man than when they are divided among several general surgeons.

DR BANCROFT C WHEELER, Worcester, Massachusetts Dr Lanman has covered his subject both clearly and completely. With so large a series of cases to support his conclusions, they bear the stamp of authority. I should like to emphasize briefly three of the points he has brought up.

In the first place, he said that surgical drainage of acute empyema is rarely an emergency. He believes that harm is more likely to result from doing a rib resection during active pneumonia than from delaying it an unnecessarily long time after empyema has developed. He presented as partial evidence the lower mortality rate and shorter convalescent period in a series of cases admitted to the hospital late in the course of the disease. Secondly, with regard to the value of irrigation he expresses frank skepticism. This is a far cry from the rigid Dakin's technique that was widely adhered to for some years after the last war, and is an agreeable simplification. Thirdly, his preliminary observations on the nature of the exudate in cases following pneumonia treated with sulfapyridine are interesting. It has been well established that neither sulfanilamide nor sulfapyridine is of much value in the treatment of such localized, walled-off pus pockets. But they are both effective in reducing the mortality of the commoner forms of pneumonia, and thereby presumably the incidence of empyema. It seems probable that the next ten years will see only a fraction of 287 cases of empyema at the Children's Hospital.

I shall present our experience with empyema in children at the Worcester Memorial Hospital during the last ten years. The series is of course much smaller than that of the Children's Hospital, but may be of interest as illustrating the occurrence and treatment of the disease in a medium sized general hospital.

Between 1929 and 1938, there were 42 cases of empyema in children. Twelve were in infants, and 30 in children from three to twelve years of age. Of the total, 25 cases

were directly due to pneumococcus, 6 to streptococcus and 4 to staphylococcus, while 5 were caused by a mixture of pneumococci and streptococci and 2 by a mixture of staphylococci and streptococci. In all but 3 the primary focus was pneumonia.

Twenty-four of these cases of empyema were treated by open drainage, 17 by closed drainage and 1 by aspiration only. Aspiration was used, however, for diagnosis in all cases and as a part of treatment in many. The case treated by aspiration alone proved fatal, as did 3 of those treated by closed drainage. The time in the hospital after drainage varied from ten days to six and a half months, but 80 per cent of the 38 living patients were discharged in six weeks or less.

Of the 4 fatal cases, 2 had a trocar thoracotomy performed during the course of active streptococcal pneumonia, 1 with a positive blood culture, and might have fared better if aspirations had been continued for a longer period. A third patient, admitted on the tenth day of pneumonia, died on the third hospital day, following two aspirations. The fourth case was that of a two-and-a-half year-old child who had been ill for three weeks. Aspiration was unsuccessful because of the tenaciousness of the pus, and the patient died, in spite of a thoracotomy, on postmortem examination meningitis was found to be present.

DR GEORGE A MOORE, Brockton, Massachusetts I am interested to know what Dr Lanman's experience has been with sulfapyridine in empyemas due to pneumococci. During the past winter I saw two patients with pneumococcal empyema who had been treated successfully with sulfapyridine during the pneumonia which preceded the empyema. Both cases were treated by aspiration in the early days of the development of empyema, with no untoward results. When it became necessary to resort to catheter drainage, both patients had a rather marked rise in temperature, which was controlled by the use of sulfapyridine, and both made satisfactory recoveries.

DR RICHARD H OVERHOLT, Boston I should like to add my approval of the general practice and plan that Dr Lanman has outlined for the various procedures. I should like to ask whether a study has been made of symptoms in the patients in this series which might indicate the nature of the underlying pulmonary lesion. We are too often asked to see patients who have developed bronchiectasis or occasionally bronchial fistulas following treatment, and in view of the excellent results reported, I am curious to know how many patients developed bronchopleural fistulas or evidence of bronchiectasis or pulmonary abscess that might require a subsequent resection of the involved pulmonary tissue.

DR LANMAN In answer to the question regarding treatment with sulfanilamide and sulfapyridine, I will say that no cases in this series were so treated. Sulfapyridine had not come into use until after its close. However, we have since that time had 6 cases of empyema developing in patients who had been treated with sulfapyridine during their pneumonia. In 4 cases the exudate in the lung was very thick and was difficult to clear up. In 1 case, as soon as the administration of sulfapyridine was stopped the temperature went up but came down when the drug was resumed. This continued for about six weeks, when it became necessary to do a very wide and open drainage. As a result, the empyema finally cleared up.

I did not say much on this subject because we have not as yet collected sufficient evidence of the value of sulfapyridine in empyema, or any accurate figures as to how

many patients develop empyema when they have had either sulfanilamide or sulfapyridine during the course of their pneumonia.

In answer to Dr. Overholt's question this series did not concern itself with cases of bronchiectasis. I have been unable to find in the series of cases treated by primary rib resection any that developed symptoms suggestive of communicating pulmonary infection. We are now studying the records in a large series of cases of pneumonia with special attention as to whether there was at the time of the

pneumonia some unrecognized atelectasis. Some of these patients had empyema associated with the pneumonia but many others did not. On the evidence we now have at hand it would seem that the development of bronchiectasis is more likely to be the result of an unrecognized atelectasis than of the empyema. We realize of course that there are many other factors, some as yet unknown that cause bronchiectasis. Cases of pneumonia with empyema that have been complicated by lung abscess or bronchial fistula may go on to chronic pulmonary suppuration.

ROULEAUX FORMATION IN FRESH, UNMODIFIED BLOOD AS A DIAGNOSTIC TEST FOR HEMOLYTIC ANEMIA*

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BOSTON

IN THE course of recent studies on the nature of the hemolytic anemias, it was demonstrated that spherocytosis of the red blood cells was in most cases a constant feature.^{1,2} Further studies now in progress indicate that this tendency of red cells to become small, thick and spherical is dependent on the action of various hemolytic agents on mature erythrocytes, and not on an abnormal formation of red cells in the bone marrow.³ Spherocytosis may thus be considered an indicator of hemolytic activity. This abnormality is by no means pathognomonic of congenital hemolytic jaundice, being found in various hemolytic syndromes.⁴ Previous studies by Haden,⁵ Boros,⁶ Heilmeyer⁷ and Castle and Daland⁸ have shown that the spherocyte is a fragile red blood cell and that its behavior in hypotonic solutions of sodium chloride can be directly correlated with its thickness. As the cell becomes thicker its diameter diminishes, although its volume remains constant. Various methods have been utilized for the estimation of the degree of spherocytosis or increased thickness of the average red blood cell. Thus the mean corpuscular thickness is determined from the knowledge of three factors: the hematocrit reading, the erythrocyte count and the mean diameter of the cell. Thus

$$\text{Thickness} = \frac{\text{Hematocrit reading} \times 10}{\text{Red blood cells in millions}} = \frac{\text{Mean corpuscular volume}}{\pi \left\{ \frac{\text{Cell diameter}}{2} \right\}^2} = \frac{\text{Mean corpuscular area}}$$

An example for a normal blood is as follows

$$\text{Thickness} = \frac{46 \times 10}{50} = \frac{92}{44} = 2.1 \text{ microns}$$

$$3.14 \left\{ \frac{7.5}{2} \right\}^2$$

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The normal mean corpuscular thickness is about 2 microns. Heilmeyer⁷ makes use of the thickness diameter (T/D) ratio in expressing the degree of thickness. This index serves graphically to illustrate increases in thickness of the red cell. The normal T/D ratio is about 1.4, with spherocytosis this ratio becomes abnormal and may reach

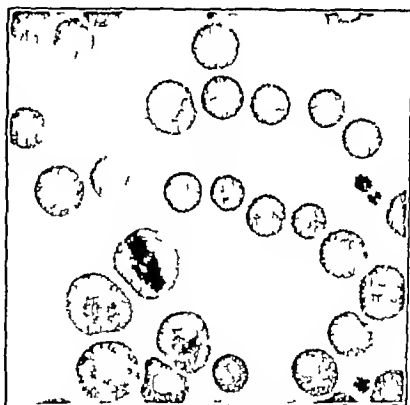


FIGURE 1 Cells from a Case of Acute Hemolytic Anemia. Photomicrograph of a stained blood smear. The small dense-appearing red cells usually without central achromia are spherocytes. The contrast in the size of these cells as compared with the comparatively large reticulocytes is readily apparent. ($\times 1350$)

levels of 1.25 or 1.2. Another method of estimating thickness indirectly is by performing the fragility test with solutions of hypotonic sodium chloride.

Direct observation of red cells for thickness has not been utilized so often as it should and it is the purpose of this paper to point out the useful

ness of this procedure. Although a stained preparation demonstrates certain characteristics of the spherocyte, namely diminished size, absence of central clear space and an increased depth of coloration (Fig 1), it can give only presumptive information. In a fresh preparation of blood which

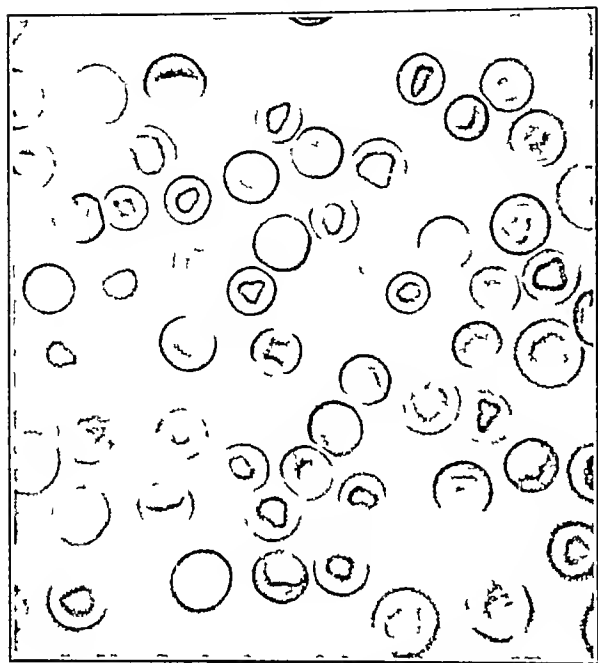


FIGURE 2. Normal Red Blood Cells

Photomicrograph of a fresh wet preparation, using Dameshek's platelet stain. In this isotonic solution containing sodium citrate, the individual red cells and their varying degrees of thickness can be observed. Note the cup-shaped and spherical red cells. ($\times 1000$)

has been prevented from clotting (as by the use of Dameshek's⁹ platelet-reticulocyte solution), the various degrees of spherocytosis in the individual erythrocytes are readily noted (Fig 2), as the red cells are frequently observed on edge. The first stage in increased thickness is the loss of one of the biconcavities of the cells, they become cup-shaped, then jug-shaped. The stage closest to the complete spherocyte is that of a small, round cell with a dimple at one end, the final stage is that of complete spherocytosis (microcytosis).*

A simpler method, and one which often gives somewhat more information, especially as regards thickness and the thickness-diameter relation, is the observation of rouleaux formation in fresh preparations of blood. When a drop of blood is placed on a cover slip, which is then dropped on a slide, the red cells form aggregates, or rouleaux, consisting of a varying number of cells in close approximation and resembling a pile of coins. The size of the aggregates and the closeness of the ap-

proximation depend in large part on the chemical status of the serum.[†] In the process of aggregation the pliable red cells apparently lose one of their biconcavities, so that one cell fits snugly into the concave portion of its neighbor. Close inspection of the rouleaux reveals that the cells are quite uniform in thickness, although some variation in size is readily apparent (Fig 3). From photomicrographs one may readily measure the thickness of the individual cells in relation to the diameter of certain free floating cells which are viewed from above. This ratio, as stated above, is normally about 1:4.

In the presence of spherocytosis the rouleaux always become abnormal. This is due to the great diversity in the thickness of the red cells and the resulting difficulty of individual cells' becoming approximated to each other. Because of this the rouleaux are hardly ever straight, rarely lengthy and often decidedly bizarre in appearance (Figs



FIGURE 3. Rouleaux Formation in Normal Blood

Photomicrograph of a fresh wet preparation. Note the long rouleaux and the approximate equality in thickness of the erythrocytes. The thickness-diameter relation can be estimated by direct measurements. ($\times 1000$)

4 and 5). The difficulty of an almost spherical cell's being closely approximated to other cells which are also thickened and rounded is obvious, and reminds one of a number of fat people trying

*The observer can readily reproduce these changes by making a fresh preparation of blood on a slide on which has been placed a pinch of pure saponin.

[†]The interesting relation of the size of the rouleaux to the fibrinogen content of the blood serum and to the blood sedimentation rate has recently been discussed.¹⁰⁻¹²

to get into a small elevator. Individual and comparative variations in erythrocyte thickness are exceptionally well brought out in these fresh preparations.

This simple test, which can be made at a moment's notice with a minimum of apparatus (glass slides and cover slips), has proved of definite value in the differential diagnosis of certain cases of anemia, particularly those in which the possibility of a hemolytic process is present. It often yields immediate information regarding such factors as the degree of spherocytosis (and indirectly of the probable erythrocyte fragility) and is thus of value in gauging the acuteness of the hemolytic process. Similar observations have recently been made by Gripwall.¹² The more fulminating a given hemolytic process, the more marked is the spherocytosis.² This is well brought

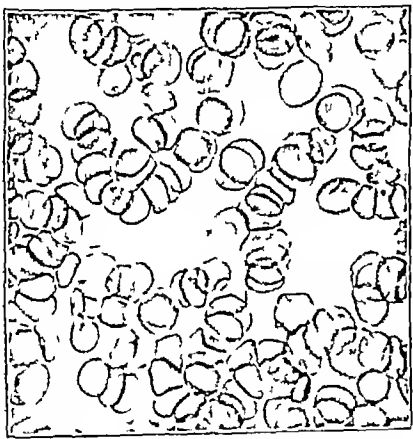


FIGURE 4 Rouleaux Formation in a Case of Congenital Hemolytic Jaundice

Photomicrograph of a fresh wet preparation. Careful inspection of various rouleaux demonstrates the generally increased thickness of the red cells and their great diversity in this factor ($\times 1000$)

out in the crises of congenital hemolytic icterus. As a preliminary diagnostic measure the test has much to recommend it, it supplements and in no wise replaces the more exact, and exacting, methods of estimating the mean corpuscular thickness, the mean diameter of the red blood cells and their fragility. Studies are now being made to determine the value of the rouleaux test for the direct measurement of red-cell thickness.

SUMMARY

The study of rouleaux formation in fresh preparations of blood is of value in estimating the presence or absence of varying degrees of thickness (spherocytosis) of the red cells. Since this abnormality is common to various types of hemolytic syndromes, the study of rouleaux is impor-



FIGURE 5 Rouleaux Formation in a Case of Acute Hemolytic Anemia and Chronic Lymphatic Leukemia

Photomicrograph of a fresh wet preparation. Note the small bizarre rouleaux, the marked variation in size and thickness of the red cells and the many small thick cells. The colorless cells are lymphocytes. Observation of a smear of this type indicates the presence of a hemolytic process with increased erythrocyte fragility ($\times 900$)

tant in the diagnosis of hemolytic anemia and in the estimation of the severity of a given hemolytic process.

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THE SYNDROME OF DIABETES MELLITUS, HYPERTENSION AND NEPHROSIS*

A Clinical and Pathological Study of a Case

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IN 1936, Kimmelstiel and Wilson¹ described a uniform pathologic lesion in the kidneys from a group of 8 middle-aged or elderly diabetic patients with hypertension who developed profuse albuminuria and generalized edema. They discussed the picture in sufficient detail to differentiate it clearly from other renal lesions. However, the discussion of the clinical findings in their series was much abbreviated. The kidneys of one of our patients, presenting this clinical syndrome, showed a similar picture. He was carefully followed during the last year of his life, during this time sufficiently numerous clinical and laboratory observations were made to define the clinical picture of this recently recognized syndrome.

CASE REPORT

J. P., a 46-year-old, white, American railroad gateman with a family history of cardiovascular disease and a past history of diabetes mellitus of 4 years' duration, controlled by diet and insulin, entered the hospital on March 7, 1930, complaining of swelling of the legs of 6 months' duration. He was quite well, except for the diabetes, until 6 months before admission, when he noted swelling of the legs, penis, scrotum and face. Two weeks before admission his arms also became swollen. He complained of nocturia once a night, at no time did he experience cough, dyspnea, orthopnea, chest pain or palpitation.

Examination revealed a well-developed and well-nourished man in no distress. The face, scrotum, penis, wrists, arms and legs were edematous. The heart was not enlarged to percussion. There was slight thickening of the peripheral arteries. A small amount of ascites was present. Ophthalmoscopic examination revealed patches of hemorrhage and exudate. The retinal vessels showed tortuosity and arteriovenous nicking. The disks appeared normal. Blood Wassermann, Kahn and Hinton reactions were negative. The basal metabolic rate was -15 and -11 per cent on two occasions. The patient was given a 1200-calorie, salt-poor diabetic diet containing 40 gm of protein. Fifteen units of insulin were also given daily. One week later the diet was increased to 1600 calories with 60 gm of protein. On this regime the patient required 15 units of insulin twice daily. Fluids were limited to 1200 cc. daily. The patient received theocin and Salyrgan on several occasions, resulting in a loss of 8 pounds. He was discharged free of edema on March 24 after having lost 26 pounds.

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He did only moderately well, and was readmitted to the hospital on April 17 complaining of weakness of the left arm and leg of 24 hours' duration. Examination revealed a slight shifting dullness in the abdomen, a small amount of fluid and a few coarse rales at both lung bases, moderate edema of the legs and weakness of the left arm and leg. The rest of the examination was similar to that on the first admission. Ophthalmoscopic examination revealed several fresh hemorrhages. The disk margins were hazy, although cupping was normal. Phenolsulfonephthalein excretion 2 hours and 10 minutes after the intramuscular injection of 6 mg. of the dye was 10 per cent. The patient showed a gradual return of strength in the left arm and leg. The diabetes was easily controlled with diet and small doses of insulin. Fluids were limited to 1200 cc. daily. The patient's face became puffy during the first week of his stay, but after several weeks all the edema disappeared. He was discharged improved on May 23, 1930, after having lost 10 pounds.

He did rather poorly, progressively becoming worse, until he was readmitted to the hospital on February 26, 1931, for the third and last time, 9 months after his last discharge, complaining of weakness and progressive swelling of the legs. He had been unable to follow his diet and receive insulin injections. The left hemiparesis continued unchanged. Examination revealed marked pallor, generalized peripheral arteriosclerosis, dullness and occasional rales at both lung bases, a small amount of ascites and pitting edema of the hands and legs. Ophthalmoscopic examination showed progression of the retinitis, with an increased amount of exudate and fresh hemorrhages. The diabetes was easily controlled with diet and small doses of insulin. The patient was given a salt-poor diet, and fluids were restricted to 1000 cc. daily. On this regime most of the edema disappeared. However, the blood non-protein nitrogen rose steadily and the patient became drowsy. Edema of the legs and signs of fluid in the chest developed shortly before death, which occurred on March 27. Bilateral thoracentesis with removal of 1750 cc of fluid was without avail.

A summary of the laboratory findings of the last year of the patient's life revealed the following. The specific gravity of thirty-nine urines varied between 1.004 and 1.032, one-half were over 1.016, during the last month of the illness it fluctuated between 1.008 and 1.018. A trace to a large trace of albumin was present in practically all the specimens. The urinary sugar was 2.5 per cent when the patient was first seen, and showed a tendency to rise between hospital admissions, the sugar disappeared while the patient was under treatment in the hospital. Acetone bodies were found in the urine on one occasion during the beginning of the period of observation. Over half the urinary sediments showed white blood cells, ranging between 1 and 10 per high power field. Hematuria was noted in a third of the examinations, the number of red blood cells ranged between 1 and 5 per high power field.

Hyaline and granular casts were present in practically all the sediments on one occasion cellular casts were observed. Doubly refractile bodies in the urine were searched for nineteen times and found on seventeen occasions on five of which large numbers were present. Serum albumin and globulin determinations were performed on fourteen occasions. The serum albumin fluctuated between 3.1 and 4.7 gm. per 100 cc. most of the values were below 4.0 gm. The serum globulin varied between 1.0 and 2.0 gm. over the determinations were below 1.5 gm. The albumin-globulin ratio was never reversed. The blood cholesterol on fourteen occasions fluctuated between 312 and 463 mg per 100 cc. The blood sugar varied with the control of the diabetic condition during the uncontrolled periods it rose as high as 488 mg. in the controlled periods it fluctuated between 72 and 133 mg. per 100 cc. The blood nonprotein nitrogen was normal during the early period of observation then became slightly elevated and in the last 6 weeks of the illness was markedly elevated, reaching a level of 117 mg. per 100 cc. terminally. The red-cell count and hemoglobin values showed a steady decline from 4,200,000 and 75 per cent respectively at the beginning of the period of observation to 3,500,000 and 60 per cent shortly before death. The systolic blood pressure varied between 144 and 210 while the diastolic fluctuated between 80 and 110. Shortly before death the blood pressure was 220 systolic, 120 diastolic.

Autopsy. Autopsy was performed 7 hours after death. There was considerable edema of the legs, scrotum and hands. A small amount of fluid was found in the abdominal cavity.

The right kidney weighed 225 gm and the left 200 gm. Both kidneys were moderately firm and pale grayish pink. The capsules were somewhat thickened and slightly adherent. The surfaces of the kidneys after stripping the capsules were finely granular. The cut surfaces were pale and grayish-yellow. The markings were well defined. The cortex was well delineated and appeared slightly narrowed, measuring 3 to 5 mm. in thickness. The pelvic fat was normal in amount. The pelvis, calices and ureters were normal. Microscopic examination revealed moderate to marked hyalinization and thickening of the media of the arterioles and small arteries of the kidneys. A moderate amount of intimal proliferation with deposit of atheromatous material was also present in the small arteries. There was marked thickening of the intercapillary fibrous tissue of many of the glomeruli (Fig 1). This was usually concentrated in the center of the glomeruli, with smaller masses of fibrous tissue extending out toward the periphery. In many areas the deposit of this fibrous material was so thick as to suggest amyloid but this was ruled out by staining several sections with methyl violet and with iodine. Sections stained according to McGregor's² technique showed the histological picture more clearly than those stained with eosin and methylene blue. The glomeruli varied a great deal in size some were of normal diameter while others were shrunken and exhibited varying degrees of diminished vascularity. Scattered glomeruli were represented by solid masses of fibrous material. In occasional glomeruli the endothelial cells were somewhat swollen but nowhere was proliferation of these cells or the production of intercapillary fibers noted. The basement membrane was slightly thickened. There was no definite crescent formation in the capsules, although they were frequently thickened. In most instances this thickening was due at least in part to the deposition of fibrous tissue. The tubular cells varied in appearance in some areas they were flat

tened and atrophic while in others they were swollen and granular or vacuolated. Many tubules contained granular material and casts. Sections stained with sudan III showed a small amount of orange stained fat in the endothelial cells of a few scattered glomeruli a moderate amount in most of Henle's loops and very large amounts in many convoluted tubules. Some of this fat was doubly refractile. The interstitial fibrous tissue was edematous and moderately increased in amount it contained a small number of irregularly distributed lymphocytes. A few of these cells were filled with fat. The



FIGURE 1 Sections of the Kidney Showing Intercapillary Glomerulosclerosis

The upper section was stained with eosin and methylene blue the lower by the McGregor technic $\times 200$

capsules of the kidneys were thickened and contained a few lymphocytes. The renal veins showed no abnormality on gross or microscopic examination.

The heart weighed 360 gm. The coronary arteries showed a moderate amount of atheroma. There was slight hypertrophy of the left ventricle the wall measuring 2.0 cm. in thickness. Microscopic examination of the heart revealed edema small areas of fibrosis and slight subintimal hyaline thickening of most of the arterioles. The lungs showed patches of bronchopneumonia. There was a small amount of irregularly distributed fibrosis and fatty infiltration of the pancreas. The arterioles and small arteries of the spleen and pancreas showed moderate in

marked hyaline thickening of the media. Slight hyalinization was observed in the media of the arterioles of the liver, adrenal glands, lymph nodes and skeletal muscle. The aorta exhibited a slight to moderate amount of atheroma. Gross and microscopic examination of the brain was essentially negative except for a moderate amount of atheromatous change in the arteries. The thyroid gland was not remarkable on gross or microscopic examination.

DISCUSSION

The pathological findings in the kidneys of the patient here reported are the same as those described in cases of "intercapillary glomerulosclerosis" by Kimmelstiel and Wilson.¹ The kidneys were large and grayish-pink, and exhibited a considerable degree of arteriosclerosis. The striking renal histological finding was the marked accumulation of intercapillary hyalinized fibrous tissue mainly in the central portions of the glomeruli, the glomerular capsules were also involved. The glomeruli were free of active or healed inflammatory changes such as occur in glomerulonephritis. A considerable degree of fatty change, including the deposition of doubly refractile bodies, was present in the cells of the tubules.

There was a history of diabetes, a recent onset of marked generalized edema, and termination in uremia. Hypertension was found early in the course of the disease. Because of the amount and distribution of the edema and the constant finding of severe albuminuria, Kimmelstiel and Wilson believed that the edema observed in this syndrome is of the nephrotic type. Our patient had profuse albuminuria, hypoproteinemia, generalized edema, hypercholesterolemia, doubly refractile bodies in the urine, a low basal metabolic rate and, early in the course of the illness, normal renal function, all characteristic of the nephrotic syndrome.^{3, 4} According to Leiter,⁴ the finding of doubly refractile lipid bodies in the degenerating tubule cells at autopsy strongly favors this diagnosis. All these observations confirm the impression of Kimmelstiel and Wilson that the edema in this syndrome is of the nephrotic type.

Hypertension and evidence of widespread arterial disease, as manifested by peripheral and retinal arteriosclerosis and signs of cerebral vascular accident, were also observed in our patient. The clinical picture was therefore not that of pure lipid nephrosis but resembled that of the nephrosis seen in glomerulonephritis or renal amyloidosis.

The clinical features of the nephrotic syndrome have been adequately described by many observers.^{3, 4} Christian⁵ pointed out that this syndrome may occur with a variety of pathologic lesions of the kidney. Cases of the nephrotic syn-

drome with degenerative lesions of the tubules and glomeruli,⁷ renal amyloidosis,⁶ glomerulonephritis⁸ and, more recently, thrombosis of the renal veins^{9, 10} have been described. To these must now be added intercapillary glomerulosclerosis, as defined by Kimmelstiel and Wilson.¹

The relation of diabetes mellitus to the pathogenesis of this particular renal pathologic change and to the clinical picture is obscure, but that it exists is attested by the fact that all the patients studied by Kimmelstiel and Wilson, as well as the one here described, had diabetes mellitus. Fishberg¹¹ recently described the nephrotic syndrome in diabetic patients in whom arteriosclerotic and arteriolosclerotic changes were found in the kidneys, glomerular lesions were not, however, included.

This syndrome of diabetes mellitus, hypertension and nephrosis is to be differentiated clinically from congestive heart failure occurring in a diabetic patient by the absence of dyspnea, cyanosis, orthopnea and venous engorgement, and by the presence of generalized rather than dependent edema. Subacute glomerulonephritis with nephrotic edema in a patient with diabetes mellitus cannot be differentiated from this syndrome clinically unless the previous history of acute glomerulonephritis is obtained. The age incidence of glomerulonephritis is quite different from that of the above-described syndrome, but this in itself need not be conclusive in differentiating one from the other. The question naturally arises as to whether the syndrome here discussed is not glomerulonephritis which has been modified clinically and pathologically by moderately severe diabetes mellitus. This question may be answered by the findings in a series of cases which have come to autopsy in our clinic and in which subacute glomerulonephritis with the nephrotic syndrome and diabetes mellitus co-existed, the microscopic renal lesions in these cases were similar in every way to those in patients with subacute glomerulonephritis with the nephrotic syndrome but without diabetes mellitus.

SUMMARY AND CONCLUSIONS

The clinical and pathological findings in a patient presenting the syndrome of diabetes mellitus, hypertension and nephrosis are presented. All the diagnostic criteria of the nephrotic syndrome were noted.

The essential renal pathological findings were identical with those previously described by Kimmelstiel and Wilson, and consisted in sclerosis of the central portions of the glomeruli and the deposition of fatty material, including doubly refractile bodies, in the renal tubular epithelium.

The relation of this type of nephrosis to others is discussed

A paper entitled "Inter-capillary Glomerulosclerosis: A syndrome of diabetes, hypertension and albuminuria," by R. A. Newburger and J. P. Peters has appeared in the December 1939, issue of the *Archives of Internal Medicine*. The findings of these authors are similar to those recorded here with the exception that there are no studies of the urine by means of polarized light and of the kidneys by means of polarized light and special stains.

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THE EFFECT OF AMPHETAMINE (BENZEDRINE) SULFATE AND PAREDINE HYDROBROMIDE ON SODIUM AMYTAL NARCOSIS*

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IN A previous study¹ on the physiologic effects of amphetamine (Benzedrine) sulfate, we noted that the duration of the narcosis produced by the intravenous administration of Sodium Amytal was distinctly shortened if a subcutaneous injection of amphetamine was given either before or after the Sodium Amytal. Since then we have studied the effect of the drug given by the intravenous route which we expected would be even more effective in counteracting the narcotic effects of Sodium Amytal. This paper records the quantitative effects of amphetamine sulfate, as well as Paredine Hydrobromide, another sympathetico-mimetic amine, on the narcosis produced by Sodium Amytal.

MATERIAL AND METHODS

A large number of co-operative, passive patients with dementia praecox were utilized as subjects. An intravenous dose of Sodium Amytal was given to each subject in an amount necessary to produce narcosis of such depth that there was no response to strong stimuli such as loud noises or face-slapping. At weekly or longer intervals each subject was given a sleep-producing dose of

Sodium Amytal followed by amphetamine sulfate,|| then both drugs simultaneously and finally amphetamine followed by the narcotic. Intravenous injections of the two drugs were always given, except on rare occasions.

RESULTS

Administration of Sodium Amytal

Seventeen subjects were given Sodium Amytal alone. It was administered slowly, at the rate of 0.1 gm. per minute. The amount necessary to produce deep sleep varied from 0.5 to 1.0 gm., the average being 0.7 gm., in some cases the amount varied widely on different occasions. A few subjects who were given the drug several times at three or four-day intervals required increasing amounts in order to produce deep sleep.

Administration of Sodium Amytal followed by That of Amphetamine Sulfate

In 19 cases deep sleep was produced by Sodium Amytal, immediately after which, or within a few minutes, amphetamine sulfate (30 to 40 mg.) was injected intravenously through the same needle. In 16 cases clear-cut awakening occurred within ten minutes after the injection of the amphetamine. In the other 3 cases it occurred in sixteen, nineteen and twenty minutes respectively. Nine of the subjects awoke within five minutes at the

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||Sodium Amytal (the trademark of amphetamine and of) and Paredine (the trademark of) were supplied through the courtesy of S. B. Kline and French Laboratories, Philadelphia.

time when the height of the reaction to the amphetamine occurred, as evidenced by the greatest rise in blood pressure, which sometimes reached

fall back into a superficial sleep. They were, however, readily aroused and were able to return to the wards with little or no assistance (Fig 1)

Simultaneous Administration of Amphetamine Sulfate and Sodium Amytal

In 5 cases the two drugs were administered simultaneously—a total of eleven experiments. The amount of Sodium Amytal given varied between 0.5 and 10 gm. The dose of amphetamine sulfate varied in most cases between 20 and 30 mg, administered intravenously, except in 1 case in which 14 mg was given intramuscularly. The amphetamine was given at the same rate as the Sodium Amytal, so that 1 cc of the former solution, containing 2 or 3 mg, and 1 cc of the latter, containing 0.1 gm, were injected simultaneously.

In no case was either superficial or deep sleep produced. Only slight drowsiness was noted. The speech of all the subjects showed thickness and ataxia. Questions, however, were answered coherently. Mild euphoria and talkativeness occurred in 3 cases. All 5 subjects were able to get off the table and dress, although with some ataxia of the legs. The blood pressure in every case except 1 showed the predominating influence of the amphetamine, the rise varying between 26 and 40 mm of mercury, in the sole exception a fall of 14 mm occurred. The effect of amphetamine

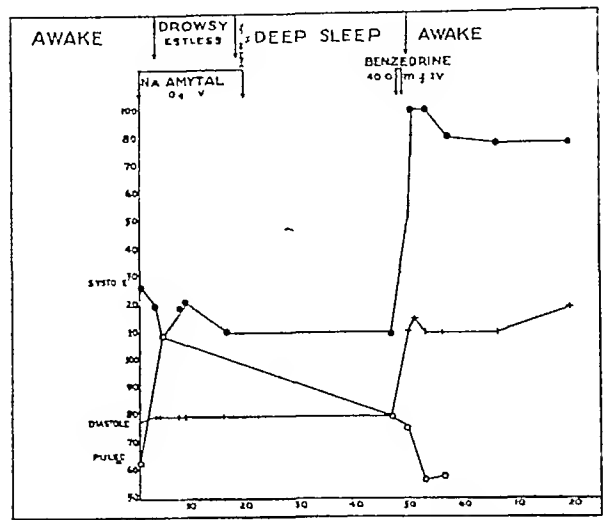


FIGURE 1 Effect of Sodium Amytal Followed by Amphetamine Sulfate

The subject awoke almost immediately after the injection of 40 mg of amphetamine sulfate

a level of 200 systolic or higher. As the effect of the amphetamine wore off the subjects appeared to become drowsy. They were, however, able to

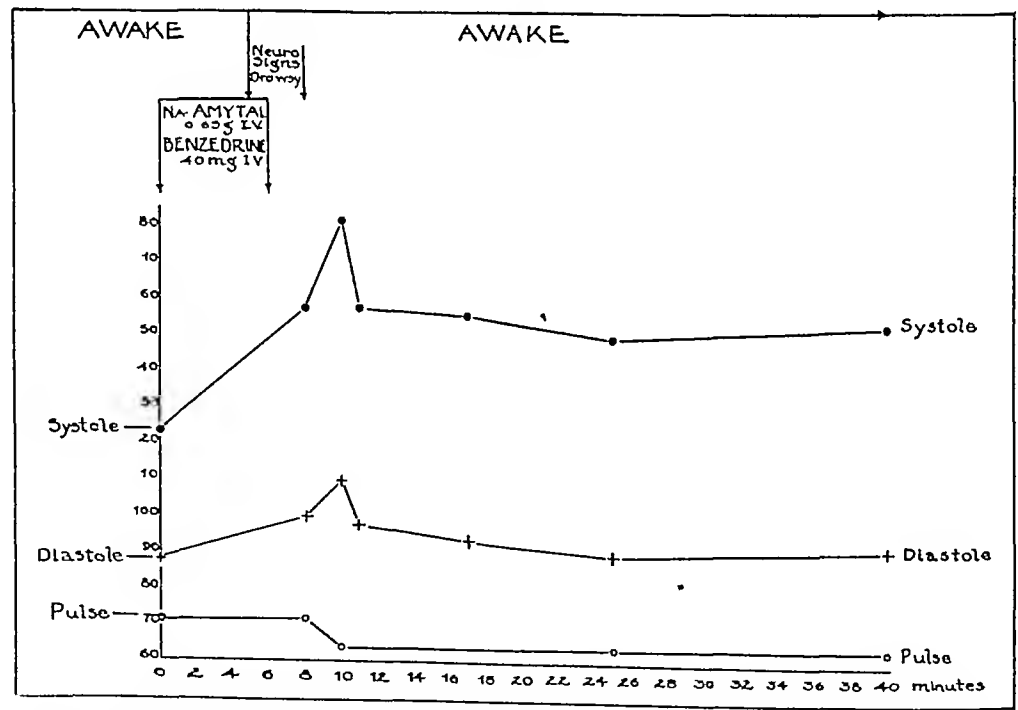


FIGURE 2 Effect of the Simultaneous Administration of Sodium Amytal and Amphetamine Sulfate
Sleep did not occur during the entire period of observation (1 hour and 40 minutes)

get off the table and walk about, with some ataxia and complaint of dizziness. Some of them, if allowed to continue lying on the table, tended to

mine on the pulse rate was predominant over that of Sodium Amytal, so that a fall of 8 to 18 beats per minute occurred, except in 2 cases in which a

rise of 4 and 8 beats respectively was noted (Fig 2)

Administration of Amphetamine Sulfate Followed by That of Sodium Amytal

In 10 cases the administration of amphetamine sulfate (30 mg intravenously) was followed by that of Sodium Amytal (0.5 to 1.0 gm) usually

Neurologic Changes

The well known neurologic changes which occur during Sodium Amytal narcosis were observed, namely constriction of the pupils, nystagmus and changes in the deep reflexes. In a few cases the knee jerks were difficult to elicit in the rest they were increased. Ankle clonus was observed in several cases, the Babinski sign was

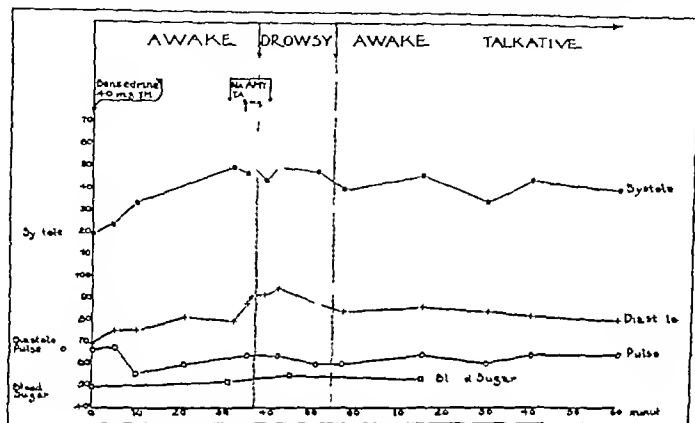


FIGURE 3 Effect of Amphetamine Sulfate Followed by Sodium Amytal
Sleep did not occur the subject was drowsy for a short period

within fifteen minutes, but occasionally as long as half an hour later. In 4 cases deep sleep lasting from five to twenty minutes occurred followed by awakening. In the other 6 cases only drowsiness was evident. Five of the latter subjects became very talkative during or after the injection of Sodium Amytal and their accessibility was quite marked. There seemed to be no direct relation in the 10 cases between the change in blood pressure and the awakening nor did it appear to make any difference in the sleep or awakening whether the Sodium Amytal was given a few minutes or half an hour after the amphetamine. In one case in which the rise in blood pressure following the injection of amphetamine was 60 mm the patient showed only drowsiness and was very talkative and lively. In another in which the rise was 40 mm deep sleep lasted for twenty minutes. In both these cases the Sodium Amytal was given within five minutes of the amphetamine. The blood pressure usually fell somewhat following the injection of Sodium Amytal but never to the original level.

The pulse rate diminished in every case during the administration of amphetamine and returned almost to its original level at the height of the reaction to Sodium Amytal (Fig 3).

never noted. On the subjects awaking from the narcosis the pupils returned to their original size. A similar phenomenon was observed when they were awakened with amphetamine sulfate. Nystagmus was invariably observed after 0.2 to 0.4 gm of Sodium Amytal had been injected, either alone or with amphetamine. The abdominal reflexes always disappeared during the Sodium Amytal narcosis, this was never noted following the giving of amphetamine alone.

When the two drugs were given simultaneously and sleep was prevented the size of the pupils remained unchanged. Amphetamine by itself had little or no effect on the neurological status. It appeared, however, to enhance the changes caused by Sodium Amytal alone. Thus, the knee jerks became more lively, and in 2 cases ankle clonus was elicited.

Effect of Sodium Amytal and Paredrine Hydrobromide

The chemical make up of Paredrine (*p* hydroxy α methyl phenylethylamine) is closely related to that of amphetamine differing from the latter in having added a hydroxyl radical in the para posi-

usually reached one or two hours after the ingestion of an alcoholic beverage. Various factors, such as the amount of alcohol consumed, the alcoholic concentration of the beverage and the presence and type of food in the gastrointestinal tract, influence the rate of absorption. The diffusion of alcohol throughout the body tissues, with the exception of adipose tissue, occurs uniformly and rapidly, although there is a skeletal-muscle lag lasting from three to four hours, as shown by Harger, Hulpieu and Lamb¹ in experimental animals. In general, however, the concentration of alcohol in the blood represents that in other body tissues, including the brain. Oxidation occurs at a uniform rate (4 to 15 cc per hr on basis of 70 kilograms of body weight), probably regardless of the amount of alcohol in the body.² Excretion is effected by two chief routes, the lungs and the kidneys, and is complete within twenty-four hours after ingestion.

CHEMICAL ANALYSIS FOR THE DETERMINATION OF ALCOHOL

Various methods are available for the determination of alcohol in body tissues, including the blood, urine, saliva and expired air.³⁻⁸ Most of these methods are dependent on the ability of alcohol to be easily oxidized in acid solution. I have had considerable experience with two methods,^{3, 4} both of which are applicable to blood and urine analyses.

In Heise's³ method the proteins are precipitated by a tartaric-picric acid solution. Distillation is carried out directly, without preliminary removal of protein. The alcohol contained in aliquot portions of the distillate is oxidized by potassium dichromate in sulfuric acid on a boiling-water bath. The concentration of alcohol is determined by direct comparison with known standards carried through the same procedure. This method is sufficiently accurate for clinical use and is time-saving, since many samples may be run simultaneously.

In Harger's⁴ method, which is also applicable to the analysis of tissues, preliminary precipitation and filtration of the proteins are necessary. The protein-free filtrate is distilled and the alcohol in aliquot samples is oxidized by standard potassium dichromate solution, positive heat of solution being obtained by the addition of concentrated sulfuric acid. Excess dichromate is determined by titration with a reducing fluid of methyl orange and ferrous sulfate. This method is more accurate than that of Heise, and by proper dilution of the reagents the so-called normal alcohol content of the fasting individual may be determined. In approximately 125 normal cases I⁹ have had

results varying from 0.007 to 0.004 gm per 100 cc (0.007 to 0.004 per cent) blood alcohol.

The alcohol in the saliva may be determined by a method devised by Friedman,⁵ and in the expired air by the method of Harger, Lamb and Hulpieu.^{6*}

SPECIFICITY OF THE TEST

Any volatile reducing substance interferes with the determination, but in the normal individual no such substances are present. Acetone bodies are reducing, but may be detected qualitatively and removed quantitatively. In a series of cases with ++++ acetone tests in the urine, the concentration in terms of alcohol was only 0.04 gm per 100 cc in both blood and urine, hardly enough to have an appreciable effect on clinical interpretation.¹⁰ Methyl alcohol has reducing properties, but may be detected in the filtrate by oxidizing it to formaldehyde and testing qualitatively for this substance. Also, the urine should be tested for formaldehyde if the subject has been receiving urotropine, since formaldehyde, a volatile reducing agent, may be produced in the kidneys. Other substances such as paraldehyde, ether, the barbiturate derivatives and acetanilid have no interfering action.

COLLECTION OF SAMPLES

In the collection of samples of blood, the arm should be sterilized with a mercuric chloride solution and wiped dry with sterile cotton. Care should be taken that no contact is made with alcohol. The best preservative is sodium fluoride, since, as Heise³ has shown, the alcohol content of blood does not deteriorate appreciably in thirty days if preserved by this substance. Addition of benzoic acid preserves the alcohol in urine indefinitely. Samples should be taken, labeled and sealed in the presence of witnesses if the case is of medicolegal significance.

CORRELATION OF CHEMICAL DATA AND ACUTE ALCOHOLIC INTOXICATION

For a correlation between chemical data and acute alcoholic intoxication, it is necessary to have some clinical criteria for the diagnosis of the condition. In a series of 1165 cases admitted to the Edward J. Meyer Memorial (Buffalo City) Hospital with a diagnosis of acute alcoholic intoxication, I¹⁰ used the following physical criteria as diagnostic:

(1) The subject must exhibit an abnormality of gait, that is staggering, swaying, reeling and so forth. If he was

*The method for determination of alcohol in the expired air is advantageous because a sample may be taken without the physical and legal difficulties encountered in taking a blood specimen. Also, a result may be obtained within a few minutes. Its disadvantages are that the apparatus is somewhat cumbersome and that sufficient data have not been accumulated correlating the amounts of alcohol in the expired air and in the blood.

in coma a follow-up study on the wards was considered essential for an accurate conclusion.

- (2) The subject must exhibit two of the following four criteria
 - a Abnormality of speech, as shown by slurring or incoherence. Trick phrases difficult to pronounce were not used. Instead, the subject was asked only familiar questions, such as inquiries as to name, residence, age and so forth
 - b Dilatation of the pupils.
 - c Flushing of the skin.
 - d Alcoholic odor in the breath

It will be realized that dilatation of the pupils and flushing of the skin are not necessarily characteristic of alcoholic intoxication. Although produced by drinking they are also found in numerous other conditions. Even an alcoholic odor supposedly easy to recognize, is sometimes mistaken for some other odor, in a number of cases it was thought to be present but a test for blood alcohol was negative. Abnormalities of gait and speech, while characteristic of intoxication may also be produced by other conditions. It was assumed, however, that if these criteria were present in the proper sequence, that is, abnormality of gait and in addition two of the other four criteria,—speech abnormality dilated pupils, flushed skin and alcoholic odor,—the clinical diagnosis of acute alcoholic intoxication was justified.

Crucism has been attached to this definition of acute intoxication on the ground that it tends to eliminate all cases but those grossly intoxicated. While this is admitted, it is believed that the criteria are easy of detection, and could be adhered to uniformly throughout a given series of cases. Furthermore, their value lies in the fact that they comprise a definite standard for the clinical diagnosis of acute alcoholism, in place of the vague term "under the influence of alcohol". The clinical interpretation of the latter would undoubtedly vary with the examiner and it is much more difficult to adhere to without variation in a large series of cases than are our criteria which are easy of recognition and interpretation.

Using these criteria for the clinical diagnosis of acute intoxication in a series of 1000 cases with alcohol in the blood¹⁸ the diagnosis was made in 47 per cent of the cases with a concentration of 0.15 gm per 100 cc., as shown in Table 1 and Figure 1. The incidence was 83 per cent at a concentration of 0.20 gm per 100 cc., and rose to 90 per cent at 0.25 gm. A total of 638 of the 1000 cases were found at these three

concentrations. At levels exceeding 0.25 gm per 100 cc., acute intoxication gradually approached an incidence of 100 per cent, which condition was reached at 0.45 gm of blood alcohol. Intoxication was usually severe at these higher concentrations, and coma was not uncommon when the blood alcohol was as high or higher than 0.35 gm. The two deaths attributed to acute alcoholism, with

TABLE 1 Number and Percentage of Cases of Acute Intoxication at Varying Levels of Blood Alcohol Concentration (1000 Cases)

BLOOD ALCOHOL CONCENTRATION gm per 100	No. OF CASES	CLINICAL DIAGNOSIS OF ACUTE INTOXICATION	
		NO. OF CASES	PER CENT
0.05	38	4	10.5
0.10	87	16	18.4
0.15	132	61	47.0
0.20	330	276	83.6
0.25	176	158	90.0
0.30	141	133	95.1
0.35	74	71	96.0
0.40	15	14	93.3
0.45	5	5	100.0
0.50	2	2	100.0
Totals	1000	40	

blood alcohol levels at 0.47 and 0.48 gm respectively, were confirmed by autopsy. No cases were encountered having a concentration of over 0.50 gm. In another series of over 800 cases,⁹ I showed a concentration above this level, namely 0.74 gm. This patient died of acute alcoholism.

A consideration of similar data obtained by other workers, namely Hoffman,¹² Widmark,¹³ and Schwarz¹⁴ in Europe and Bogen¹⁵ and Har-

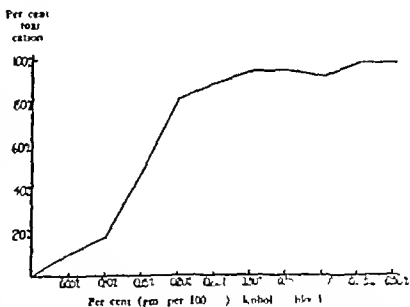


FIGURE 1 Percentage Occurrence of Clinical Intoxication at Various Concentrations of Alcohol (1000 Cases) Reproduced by courtesy of American Journal of the Medical Sciences (1964-80 1938)

The Supreme Court of Arkansas¹¹ has defined this condition as follows: "The expression 'under the influence of intoxicating liquor' covers not only the well-known and easily recognized conditions and degrees of intoxication but any abnormal mental or physical condition which is the result of the ingestion in any degree of intoxicating liquor and which tends to depress him [the subject] of that clearness of intellect and control of himself which he would otherwise possess."

ger Lamb and Hulpieu⁶ in this country, demonstrated somewhat similar results that is a rise in the incidence of acute intoxication at blood alcohol concentrations from 0.10 to 0.20 gm. per 100 cc.

However, an incidence of 100 per cent was noted at a blood alcohol concentration of 0.20 to 0.25 gm per 100 cc, whereas in the present series all individuals were not intoxicated until a level of 0.45 gm had been reached

Such a variation as that just noted is not easy to explain. It may be due in part to differences in the criteria for evaluating acute intoxication, for in none of the series previously mentioned were the criteria clearly defined. It is also believed that individual tolerance is a potent cause of this variation. For example, several subjects, all chronic drinkers, were examined and found relatively sober by all clinical tests, yet the blood alcohol concentration varied from 0.35 to 0.45 gm per 100 cc. It should be emphasized that this is a concentration close to the lethal point, and one at which severe intoxication or even coma is the common finding. That such a tolerance is not based on variability in the absorption of alcohol seems clear, since it is only the actual concentration of alcohol in the blood that is considered, and not the amount of alcohol ingested. This series, as might be expected in any large group of cases of acute alcoholism, was composed largely of chronic cases, that is, persons in the habit of consuming some sort of alcoholic drink in appreciable quantities as a daily routine. Since it is believed that tolerance to alcohol can be acquired, this factor may be expected to account for the variation in the incidence of intoxication in our series as compared with that in those previously mentioned.

This is clearly illustrated by experimental work in which a volunteer group, consisting of alcoholic neophytes or occasional drinkers, were fed alcohol.¹⁰ These subjects were examined for acute alcoholic intoxication by the same clinical criteria as those used in the larger series. All were clinically intoxicated at a blood alcohol concentration of 0.20 gm per 100 cc., as compared with the incidence of 83 per cent at the same concentration in the larger group, consisting primarily of chronic drinkers. In addition, it appeared that the occasional drinker exhibited a slight tolerance in comparison to the neophyte. Whether this tolerance, shown to the highest degree in the chronic alcoholic patient, is produced by an altered blood-brain alcohol ratio is unknown. Nevertheless, it would seem that some unknown mechanism exists in this type of individual protecting him from the severe clinical manifestations of acute alcoholism commonly found in the average person at these high blood alcohol concentrations.

ADVANTAGES OF THE CHEMICAL DETERMINATION OF ALCOHOL

In cases of coma, chemical determination of the alcohol content of the blood or urine should be as routine a procedure as are analyses for urea and sugar. For example, in 37 comatose patients referred to the Edward J. Meyer Memorial Hospital as cases of alcoholism, the diagnosis was proved erroneous by a negative blood alcohol test.¹⁰ As shown in Table 2, coma was produced in 16

TABLE 2 *Correct Diagnoses in 37 Alcohol Free Cases with a Preadmission Diagnosis of Acute Alcoholic Coma*

DIAGNOSIS	NO. OF CASES
Barbital poisoning	8
Paraldehyde poisoning	8
Fractured skull	7
Cardiovascular accident	5
Schizophrenia	2
Diabetes mellitus	2
Uremia	2
Psychosis	1
Epilepsy	1
Central nervous system syphilis	1
Total	37

cases from overdosage with either paraldehyde or barbital derivatives, while diabetes mellitus, uremia, cerebral injuries, cardiovascular accidents and schizophrenia were also found.

On the other hand, the possibility of the coma's being produced by alcohol must also be considered. For example, the police requested the admission of a man found lying unconscious in the street. After artificial respiration had been administered by firemen, the patient was brought to the hospital with a diagnosis of heat stroke. On admission the possibility of alcoholic coma was suspected. The alcoholic concentration of the blood was 0.37 gm per 100 cc. Thus the determination of the concentration of the alcohol in the blood or urine is of definite value in the differential diagnosis of coma.

It is in the medicolegal field that the chemical method should prove of greatest value, particularly in automobile accidents. First of all, it determines accurately whether an individual has been drinking. Second, from the determined concentration of the blood alcohol it is possible to estimate the approximate amount of alcohol ingested, provided that the drinking has occurred within an hour or less.¹⁰ It should be emphasized that the sample of blood required for analysis should be taken as soon as possible after apprehension, preferably within an hour. However, if the sample is not obtained within this time, the level of alcohol at the time of apprehension may still be estimated by an interpretation of the curve showing the relation

between the elapsed time after drinking and the concentration of alcohol in the blood.¹⁸

The actual blood alcohol concentration at which a person should be considered intoxicated would seem to depend on the definition one uses in diagnosing the condition. In automobile accidents, the leading cause for the arrest of alcoholic individuals, the complete syndrome of clinical intoxication, with its gross staggering, reeling, incoherence or coma, should apparently not be adopted. Actually a person at this stage of intoxication may be physically unable to drive a car, and usually does not do so. Furthermore, of a number of persons who are drinking probably only a small percentage consume enough of an alcoholic beverage to place them in this category. Nevertheless, it is these individuals who, even though not intoxicated according to our criteria, may become a menace at the wheel of an automobile.

Numerous experimental data have been accumulated tending to prove that even small concentrations of alcohol in the blood (0.04 to 0.10 gm per 100 cc) slow the reaction time, impair judgment, increase the number of errors while performing mechanical tests and so forth. Bauer¹⁷ has published a report of his work showing that the presence of alcohol in experimental subjects increased the speed at which they drove their automobiles. Heise and Halporn¹⁸ have shown in actual road tests that an individual with a blood alcohol concentration of 0.10 gm. per 100 cc., induced by the administration of 5 ounces of whisky in a short period of time, requires 50 per cent more distance to brake his car to a stop on signal than does the same individual when alcohol free. That drivers who have been drinking are more liable to be involved in accidents has been shown by Holcomb.¹⁹ He noted that 47 per cent of drivers so involved had appreciable amounts of alcohol in the blood, in comparison with only 12 per cent of a group of drivers picked at random who were not involved in accidents. Also, the average person with a blood alcohol concentration of 0.15 gm per 100 cc. was fifty five times more likely to have an accident than a driver with no alcohol in his blood. Thus it would appear that the complete syndrome of acute intoxication is unnecessary in order to make the diagnosis in automobile accident cases. Hence the term "under the influence" acquires significance.

The National Safety Council²⁰ has adopted an alcohol concentration of 0.15 gm per 100 cc. in the blood or 0.20 gm. in the urine* as inconsistent

with the safe operation of a motor vehicle, and a level at which prosecution should be conducted in automobile accidents and traffic violations. This seems logical, although it should be emphasized that even lower concentrations of blood alcohol, down to 0.10 gm per 100 cc., may be of significance in all cases except those in which tolerance has been developed to a high degree. While only 50 per cent of cases in a group of habitual drinkers will be clinically intoxicated at a blood alcohol level of 0.15 gm per 100 cc., sufficient impairment of faculties will be present in even this type of individual to make him a menace as a driver. However, it should be remembered that this type of drinker forms only a small portion of the general population, and because of his alcoholic tendencies is likely to be of so low an economic status as to eliminate him from the car owner and driver class. It is rather the alcohol neophytes and the occasional drinkers with a relatively low tolerance who form by far the largest group involved in motor accidents. In any case, a blood alcohol concentration of 0.15 gm per 100 cc. represents an appreciable consumption of an alcoholic beverage, as the average person weighing 70 kilograms must ingest 6 or 7 ounces of 100-proof whisky within an hour in order to attain this level.²¹

* * *

The value of the chemical method in the detection of intoxication is evident. The difficulties of proving satisfactorily to a court and jury at some later date that a given individual was "under the influence" on clinical findings alone are notorious. While the defendant seldom contends that he has had nothing to drink, he usually has witnesses who testify that he was thoroughly sober at the time of arrest and had taken only a small quantity of liquor, for example one glass of beer. Furthermore, the shock of an accident, the sobering effect of the arrest and the apprehension felt while awaiting trial may so affect the defendant as to cause doubt in the examiner's own mind as to the part that alcohol played in the accident. The chemical test would do much to clear up these difficulties, both in a positive and a negative sense, since it shows whether the individual has been drinking and more important the approximate amount of liquor that must have been consumed.

The value of the chemical determination of alcohol in the blood and urine lies in the fact that it is an added weapon in the diagnosis of inebriation, but it should be supplemented whenever possible by such physical data as can be collected by a competent observer. It should not be assumed that the chemical method makes clinical evaluation obsolete; rather it should be considered an

In a series of 372 cases in which simultaneous examinations of the blood and urine alcohol were performed, the ratio of blood alcohol to urine alcohol was 1:1.32. At the higher concentrations of alcohol the ratio tended to approach unity whereas at low concentrations it varied considerably. A fair assumption could be made from this work, however, that an alcohol concentration of 0.20 gm. per 100 cc. in the urine represents at least 0.15 gm. in the blood.

other means of arriving at a proper interpretation of certain physical and mental abnormalities which may or may not have been produced by alcohol. A combination of the chemical and the physical examinations should offer a better chance for the detection and conviction of the inebriated than is afforded by either method alone. It is to be hoped that legislation will be passed which requires the addition of the chemical method in the diagnosis of suspected alcoholic intoxication.

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REPORT ON MEDICAL PROGRESS

CURRENT EPIDEMIOLOGICAL ASPECTS OF SCARLET FEVER*

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SCARLET fever today is just about as prevalent as it ever was. The general level of severity, however, has progressively decreased over a long period of years. Experienced clinicians recognize these facts, and they are substantiated by the prevailing low case fatality and mortality rates in the world at large. The fewer deaths from scarlet fever that occur now as compared with a half century ago are related but little to improved methods for prevention and control. A good deal of this change is due to a better level of general health conditions, a factor difficult to measure but undoubtedly real. Better methods of medical management for those who become ill have contributed materially to the lower case fatality. Probably the most important influence is the existing favorable state of equilibrium between host and parasite. How much of the latter is dependent on greater community resistance from increased numbers of inapparent and atypical infections, and how much is directly concerned with altered biologic activities of the infectious agent that have presumably taken place in the past

sixty years, is difficult to determine. Neither is it possible to venture much of an opinion as to how stable is the present equilibrium or how permanent it may be. There is need for better definition and explanation of the epidemiological relations involved in the behavior of this disease, if improved control measures are to be developed that may lead to as favorable an influence on incidence as has occurred in respect to deaths.

Our conception of scarlet fever as a disease has undergone material change in the past several years. This started with the contributions of Dick and Dick¹ and of Dochez^{2,3} in 1924, which served to reopen the whole question of the part that streptococci have in the causation of scarlet fever. These studies, and the many that followed shortly thereafter, resulted in almost universal agreement that the infectious agent responsible for the disease belongs to the group of hemolytic streptococci. The extensive laboratory investigations since then have had the usual effect of a better appreciation of epidemiological problems that ordinarily comes from greater knowledge of the infectious agent.

The principal epidemiological advances have come from application to field investigations of

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newly developed laboratory methods for the study of hemolytic streptococci. These studies have been concerned not only with scarlet fever itself but with other clinical conditions caused by this infectious agent. Interrelations have been defined that have led to an interpretation of scarlet fever as being but one of the multiple manifestations of hemolytic streptococcus infection in man, distinguished from the others by the addition of toxic manifestations to the ordinary reactions of tissue invasion that characterize streptococcal disease in general (Okell⁴ and Griffith⁵). What has long been considered a specific infectious disease, in the sense of cholera and plague, now appears to be a disease syndrome caused by any one of a wide variety of hemolytic streptococci. The factors that determine whether scarlet fever or simple streptococcal infection is to develop are two individual and variable characteristics, one related to the host and the other to the parasite. That of the infectious agent is the capacity to produce erythrogenic toxin, that of the host, the presence or absence of specific resistance to this toxin.

Several kinds of evidence may well be examined in order to determine how well this conception is justified. Is it in agreement with our clinical knowledge of scarlet fever? Does it coincide with observed information about hemolytic streptococci in scarlet fever and in other diseases? And is it compatible with the epidemiologic behavior of the disease?

CLINICAL NATURE OF SCARLET FEVER

Some communicable diseases occur almost invariably as a frank, well-marked attack presenting classical manifestations wholly typical of that disease. Others show extreme differences in clinical reaction sometimes seeming to shade off almost unendingly to present such slight host-parasite reactions that the effect is beyond clinical observation, and becomes latent or subclinical infection. Scarlet fever has always been known for its erratic behavior. Erasmus Darwin described the disease as being anything from a flea bite to the plague. Critical examination of even the most extreme clinical forms of scarlet fever gives indication of a syndrome having two components. Certain signs and symptoms can be related to the effects of a toxin others depend on the septic, infectious or invasive properties of the agent (Cooke⁶). Both can be recognized in varying degree in all forms of classic scarlet fever, the common clinical classification of the disease being largely based on the differences in proportion of toxic and septic elements. Thus, a clinical type exists in which the manifestations are essentially toxic, still another in which septic

influences predominate, and a third mixed form which is the usual manifestation of outspoken scarlet fever, and is variously designated as mild, moderate or moderately severe. Aside from this group of readily recognized reactions, there is a group of atypical infections of varying extent, mild in nature and difficult to diagnose. They represent essentially low grade invasive reactions with the toxic element indefinite and sometimes so slight that the eruption of the skin is most fleeting. The third general form of infection is latent or subclinical. The toxic element is absent and the invasive factor so slightly active that it leads to no clinically recognizable signs. There is clear-cut evidence of the existence of this group but little appreciation of the number of cases involved in proportion to the other two.

The septic component of the scarlet fever syndrome is present in all recognizable infections. The signs and symptoms result from invasion of tissue, and are like those of all other streptococcal disease, being essentially the same whether the part involved be the pharynx and tonsils as in scarlet fever, the skin as in erysipelas, skeletal muscle as in wound infections or the mucous membranes as in puerperal fever or simple meningitis. There is malaise, fever, leukocytosis and the reaction of inflammation from lesions in local tissue. There is a tendency to spread by extension to neighboring structures—to the endometrium in puerperal fever, to the middle ear and lymph nodes in scarlet fever and to the lymphatics after surgical infections. The complications of scarlet fever so outstanding a feature of the disease, are strictly a part of the septic component, and mark an ability of the streptococcus to multiply locally and to invade tissue.

The toxic component of scarlet fever is related principally to constitutional effects in contrast to the local disturbances resulting from septic action. It is responsible for the exanthem and the enanthem and for the constitutional reactions marked by vomiting, generalized lymphadenopathy, arthralgia and albuminuria.

Together these two components constitute the syndrome scarlet fever. Considering scarlet fever generally their relative emphasis varies greatly. In the individual case the preponderance of one component over the other depends on two variants. The first is the relative ability of the streptococcus concerned to form a soluble erythrogenic toxin. The other is the degree of specific resistance possessed by the host, as determined by the content of streptococcal antitoxin in the blood. Thus, infection with a streptococcus that produces erythrogenic toxin can lead to two kinds of clinical reaction. The result in a Dick negative subject—a

host with antitoxic immunity — is a local infection, corresponding to sore throat or tonsillitis. A Dick-positive subject, lacking antitoxic immunity, develops the complete syndrome of scarlet fever. Infection with a streptococcus unable to generate rash-producing toxin gives only a localized throat infection, irrespective of whether the host has antitoxic immunity or not. It follows, then, that the rash in scarlet fever infection is a fortuitous circumstance, depending on the coincidence of two variable factors, and that scarlet fever differs only from other streptococcal infections in that a toxic element is added to the signs and symptoms of septic infection which characterize all disease due to these micro-organisms. The presence of toxic symptoms is essential to the clinical recognition of scarlet fever infection, its absence does not eliminate that possibility.

The relative importance of these two components from the standpoint of resulting death and disability is of practical significance. Logically a combination of the two should lead to a more serious effect than the presence of one alone. Furthermore, it is conceivable that toxic effect may favor invasion, although precise evidence of any significant relation is lacking. It is well known, however, that most deaths from scarlet fever, as it currently exists, are the result of complications and but little related to acute toxic action. The frequency and extent of complications depend largely on the ability of the micro-organism to invade tissue. Detailed studies of the frequency of complications in streptococcal infections, with and without toxic manifestations, seem to indicate little actual difference. Stebbins, Ingraham and Reed,⁷ in their study of mixed epidemics from milk-borne infection, found complications essentially as frequent in persons who had no rash as among those who did. Hobson's⁸ observations in England led him to the conclusion that complications were even more frequent when rash was absent than when it was present.

The mechanism of resistance on which recovery from scarlet fever depends is apparently of a dual nature. The ability to prevent growth and progressive invasion of tissue depends on antibacterial protection. Neutralization of toxin is a function of antitoxic resistance. That one type of reaction may have some influence on the other — a high degree of antitoxic immunity contributing to protection against tissue invasion — seems possible, although it is not clear to what extent or in what manner (Maxcy⁹). The unusual cases in which Dick-negative nurses and physicians have had repeated and long-continued exposure before contracting scarlet fever suggests the opposite situation — of resistance to infection with-

out antitoxic immunity — and that the resistance is local and not dependent on circulating antibodies, at least not on antitoxin.

SCARLET FEVER AND OTHER HEMOLYTIC STREPTOCOCCUS DISEASES

Recovery from even the mildest forms of scarlet fever almost invariably gives protection against a second similar attack, combining infection with toxic manifestations. The likelihood of a subsequent angina from infection with a strain of hemolytic streptococcus capable of producing the syndrome with rash in a susceptible host is by no means eliminated. Naturally acquired antitoxic immunity is usually permanent, but the resistance to invasion of tissues is decidedly temporary.

Clinical and epidemiological records of cases of scarlet fever contain repeated indications that streptococci recovered from them cause other kinds of infectious disease. Factual evidence came from the studies of Stevens and Dochez¹⁰. Field studies in Detroit (Gordon et al.¹¹) showed a well-marked frequency of coincident sore throat or upper respiratory infection among family contacts of patients with classic scarlet fever. Remarkably similar results were reported by Ramsey¹² from comprehensive studies in New York State.

Immunologically identical strains of hemolytic streptococci have been repeatedly isolated from the members of a family having angina, some with and some without skin eruption. Other field studies have shown the probable introduction of scarlet fever into families by a member who first developed simple angina, since the hemolytic streptococci from both infections were serologically identical, were usually of a type uncommonly encountered in sporadic sore throat, and sometimes had previously been unrecognized in that community.

One of the best illustrations of the epidemiological relation of scarlet fever to other streptococcal infections of the upper respiratory tract is that reported by Stebbins, Ingraham and Reed.⁷ In milk-borne outbreaks of hemolytic streptococcus infection, some persons contracted classic scarlet fever, others developed simple angina, and sometimes there was erysipelas. The relative proportion of hemolytic streptococcus infections with and without toxic manifestations varied from epidemic to epidemic, but both were represented in a given outbreak. In the Wellsville outbreak, for example, 65 per cent of 196 patients had no eruption of the skin, and this was the only essential difference in respect to all patients. The degree of fever and the proportion of complica-

tions were about the same in those both with and without rash. Infections were essentially as frequent among persons with a history of scarlet fever as among those without. Dick tests made after the epidemic had subsided showed the percentage of those reacting negatively to be somewhat greater if the illness had presented the symptoms of scarlet fever than if the clinical manifestations were those of septic sore throat. McLean¹² in Canada, reports a mixed outbreak of scarlet fever, epidemic sore throat and tonsillitis, where in tonsillitis and scarlet fever were commoner among children, and septic sore throat among adults.

Another kind of evidence lends strong support to the experience gained from the study of outbreaks and from the reactions of family contacts. By the time adult life is attained about four of every five persons have become Dick negative (Zingher¹⁴), with relatively few having an intervening history of a rash characteristic of scarlet fever. This suggests that infections with toxigenic streptococci that lack rash are much more frequent than those having this toxic manifestation.

This clinical and epidemiological evidence naturally brings to the private practitioner in medicine the important question as to what interpretation is to be made of streptococcal angina with out rash and what procedure is indicated in respect to family contacts and the protection of the public health. It should be apparent that both patients with angina and rash and those who develop only angina from contact or association with them should be considered as having scarlet fever infection. Both infections are probably due to strains of hemolytic streptococci capable of causing the usual scarlet fever syndrome.

The sporadic case of streptococcal angina or tonsillitis, under present circumstances is interpreted as an ordinary streptococcal infection. The laboratory methods currently available for determining whether or not the particular strain produces an erythrogenic toxin are too complicated for clinical application. Such an interpretation rests on necessity, with full realization that such sporadic infections are sometimes more than simple angina due to a non-toxicogenic streptococcus and that the organism concerned may produce scarlet fever if transmitted to a susceptible person. When sore throat occurs in epidemic proportions, some cases of recognizable scarlet fever are certain to occur if the infectious agent is toxigenic.

It is important to realize that recognition of scarlet fever infection many times depends as much on epidemiological as on clinical methods of diag-

nosis. Improved results in control are scarcely possible until equal attention is devoted to hemolytic streptococcus infections etiologically identical but clinically divergent.

DIFFERENTIATION OF HEMOLYTIC STREPTOCOCCI

Only those strains of streptococci that are hemolytic and produce erythrogenic toxin are concerned in scarlet fever. Not long after the description of this toxin by Dick and Dick,¹⁵ it became apparent that hemolytic streptococci from a number of other conditions, notably erysipelas (Birkhaug¹⁶), could produce a soluble toxin and that this was not a characteristic limited to strains isolated from scarlet fever patients. Long continued investigations by a number of workers in different countries (Kirkbride and Wheeler¹⁷, Eagles,¹⁸ Smith¹⁹, McLachlan⁶ and Fraser²¹) brought out other relations. Not infrequently strains producing strong erythrogenic toxin were isolated from conditions entirely apart from scarlet fever. It was learned furthermore, that strains from scarlet fever varied greatly in the amount or strength of the toxin they could form, although as a rule hemolytic streptococci from non-scarlatinal sources produced weaker toxins than did those from scarlet fever. The most important demonstration however was that most erythrogenic toxins, whatever their source could be neutralized by a single antitoxin obtained from animals injected with the well known strain—NY 5 (Fraser²¹). If two other antitoxins were used almost all known toxin-producing strains could be separated into one of three groups: a principal group including about 85 per cent of the strains, and two minor divisions. This work brought out that it is impossible either qualitatively or quantitatively to mark off toxigenic strains obtained from cases of scarlet fever from those found in other conditions.

Much effort has been given to other possible methods for differentiating the hemolytic streptococci which are responsible for the disease, scarlet fever. Important progress was made when Lancefield²² prepared a chemical fraction called "C substance." Using this material as antigen she divided the hemolytic streptococci into several groups, designated as A to G, a series subsequently enlarged by the studies of Hare³ to include Groups H and K. From these investigations came the very useful information that the great bulk of hemolytic streptococci producing disease in man fall into Group A, that strains from Groups F, G and sometimes C are occasionally involved, but that, for practical purposes, the separation of hemolytic streptococci on the basis of whether they are pathogenic or non-pathogenic for man depends

on their identity with Group A. Since almost all strains from all forms of human streptococcal infection belong to Group A, the method gives no direct aid as a possible means of separation of scarlet fever strains from those in other conditions. A method for subdivision within Group A was essential.

Many years before Lancefield's recognition of groups, Dochez, Avery and Lancefield²⁴ had been able by mouse-protection tests to recognize several serological types among streptococci concerned with human disease. Evidently these represented types within Group A. Bliss,²⁵ Eagles,¹⁸ Gordon²⁶ and others studied the possibility of distinguishing types by serological methods, principally that of agglutination. In 1928 Lancefield²⁷ made another valuable contribution in demonstrating a type-specific "M substance" within members of Group A. By precipitin technic she separated a number of immunologically distinct types. About the same time, Griffith²⁸ developed an improved method for type differentiation of Group A streptococci by agglutination with absorbed serums. In all, he has distinguished twenty-six types, with a few additional ones as yet unconfirmed. Still other types probably exist, but the extent of type differentiation within the group has probably been quite well defined, because the material studied has been drawn from many different clinical conditions and is of broad geographical distribution.

These improved methods led to work on the problem of whether a single kind of hemolytic streptococcus was regularly concerned in scarlet fever, whether a limited group was involved, or whether any one of the known serological types could at times have a part in causation of the disease. Andrewes and Christie²⁹ long ago came to the conclusion that no single serological type was involved. Griffith and Gunn³⁰ found that most scarlet fever strains from England belonged to Griffith's Types 1 to 4, and that while there was relatively wide distribution through his other types, the numbers concerned were small. Equally important was the observation that similar type strains could be isolated from non-scarlatinal infections. Other English workers confirmed these studies. As the methods were taken up in other countries,—in Australia (Keogh et al.³¹), China, most of Europe and some parts of America (Bailey,³² Pauli and Coburn³³),—it gradually developed that while most cases of scarlet fever in a given area were related to a limited number of types, nevertheless the types comprising the group varied appreciably from region to region. Practically all the twenty-six recognized types have been found somewhere in the throats of persons

with scarlet fever. Furthermore, the many types found in scarlet fever were isolated from time to time from cases of acute tonsillitis, septic sore throat, puerperal fever, erysipelas and a variety of other infectious diseases. Occasionally type strains ordinarily concerned with the production of disease could be found in the throats of apparently normal people. The belief becomes more and more generally accepted that no special kind of streptococcus, distinguished either by its ability to produce erythrogenic toxin or by serological differences, is characteristic of scarlet fever, and that no limited number of serological types is involved, although in a given locality certain ones almost invariably predominate.

From what has been said, it is evident that the mere demonstration of hemolytic streptococci in the throats of persons suspected of having scarlet fever is of itself without value in diagnosis. Clinical and epidemiological evidence must decide this, except that the presence of hemolytic streptococci in appreciable numbers is compatible with the diagnosis of scarlet fever, and that their absence strongly discounts that possibility.

EPIDEMIOLOGY OF STREPTOCOCCAL INFECTIONS

The existing epidemiological problems in scarlet fever seem, then, to resolve into the epidemiology of beta hemolytic streptococcus infection in general. The clinical manifestations of the disease merge into related conditions. This can be demonstrated by field and laboratory studies for individual cases and for groups of cases.

Many epidemics characterized by a predominance of infections with rash have begun with cases of simple angina and upper respiratory infection. Characteristically, classic disease with typical eruption dominates the peak period, with the outbreak frequently tapering off into a variety of atypical and dissimilar infections. The expectancy in sharply defined outbreaks of scarlet fever is a single serological type of hemolytic streptococcus as the infectious agent. Endemic conditions are characterized by a wide variety of types, with some three or four usually predominating. This applies particularly to the scarlet fever that is more or less continuously present in large cities. The clinical nature of the disease as it occurs in a given outbreak is greatly influenced by the relative toxicogenicity and the invasive qualities of the particular strain. Most cases in outbreaks due to types with marked ability to produce toxin, such as Type 10, have classic scarlet fever, with relatively few atypical infections and cases of scarlatinal angina. Epidemics caused by a weak toxin-producer, such as Type 18 may be, are known to include few cases of skin erup-

tion and roughly twenty times that number of sore throats. In epidemics with scarlet fever and scarlatinal angina both fairly frequent, the distribution is characterized principally by sore throats among adults and by scarlet fever among children. Explosive milk-borne outbreaks, originating from a single exposure often include scarlet fever, tonsillitis and erysipelas as clinical manifestations of infection, indicating that outbreaks tend to breed true according to the streptococcus involved, but not according to clinical disease. Outbreaks of acute respiratory disease of a virus nature—such as measles or influenza—at a time scarlet fever is current can exert a profound influence in extending and quickening its spread. Epidemiological history further reveals repeated episodes in which an outbreak of scarlet fever has been preceded by one of colds or influenza, the two acting independently, but suggesting that the genesis of the scarlet fever outbreak may have been largely conditioned by the preceding epidemic of virus disease.

The principle seems well defined that a program of investigation and control of scarlet fever must deal with the whole group of hemolytic streptococcus infections: it is a streptococcal problem and not one of rashes. Many will ask how necessary is increased emphasis on the control of scarlet fever, with the disease as mild as it is. That depends on what the future holds in respect to scarlet fever and the answer to that question is wholly speculative. In most parts of the world today scarlet fever is a mild disease, with deaths less than 5 per cent of what they were eighty years ago. The reports of Pope,³⁴ and of Wilson, Bennett, Allen and Worcester³⁵ making use of the long-continued observations in Providence, Rhode Island, show that in 1865 the mortality from scarlet fever in that city was 261 per 100,000. In 1937 the mortality was 2.9 per 100,000.³⁵ In 1886 about one of every five persons who contracted scarlet fever died. The present ratio is about 1/120. How long this favorable situation will last, no one knows. Extreme variations in severity have occurred and there is no reason to believe that they will not recur. During the middle of the seventeenth century Sydenham described scarlet fever as extremely mild. It changed character toward the end of the eighteenth century to become a very severe disease. In London from 1804 to 1816 it was again mild, but after 1830 it again became a leading cause of death in childhood continuing so until the middle of the nineteenth century, when the present progressive downward trend came into play. Knowledge of what to expect in the future may well be aided by

more information in respect to some of the epidemiological problems, which are becoming increasingly better defined and appreciated.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 25521

PRESENTATION OF CASE

A seventy-eight-year-old widow was seen by her physician because she was extremely nervous and mentally disturbed following an attack of vomiting. On examination she had a temperature of 101.5°F, a pulse rate of 92, a red throat and an occasional fine rale in both chests. On examination her heart was within normal limits, a systolic murmur was heard over the whole precordium. There was an occasional extrasystole. The left patellar reflex was slightly greater than the right. The other tendon reflexes were normal. A blood smear showed an elevated polymorphonuclear count but was otherwise negative. A diagnosis of a mild respiratory infection was made.

The patient was seen again two months later because of increasing nervousness. Her physical examination at that time was essentially negative. The blood pressure was 145 systolic, 95 diastolic. A year and a half later she was examined because of easy fatigability, occasional shortness of breath and slight orthopnea, she used two pillows at night. The heart was then found to be 9 cm. to the left and 3 cm. to the right of the median line. There was marked accentuation of the aortic second sound, and moderate accentuation of the pulmonic second sound. A short systolic murmur was heard over the whole precordium. The pulse rate was 96, and the blood pressure 140 systolic, 80 diastolic. The lung bases were clear, the liver edge was not palpable, there was no edema of the ankles.

Fifteen months later she was seen following an attack of "grippe" that was accompanied by persistent pain in the lower ribs which lasted about six days. Physical examination revealed increased anteroposterior diameter of the chest with hyperresonance, except at the left base below the midscapular region where there was slight dullness, and vesicular breath sounds throughout with no rales but slight decrease in intensity below the angle of the left scapula. The border of dullness of the heart was 8 cm. to the left of the mid-line in the fifth interspace and 3.5 cm. to the right in the fourth. The sounds were distant but clear. There were no murmurs. The blood pressure was 130 systolic, 80 diastolic, in both arms and 150 systolic, 90 diastolic, in both legs. There

was no tracheal tug. The pupils were equal and reacted to light and accommodation. The peripheral vessels showed a rather marked degree of peripheral arteriosclerosis. Portable chest plates showed a large round mass, apparently continuous with the heart shadow, occupying the entire middle third of the left lung field. An electrocardiogram showed a sinus tachycardia of 135 beats a minute, with left-axis deviation (-22°), a PR interval of 0.13 sec. and notched P₃ and P₄, QRS₁ and QRS₂ were of fairly low voltage (6 mm. and 5 mm. respectively), ST₁ and ST₂ sagged slightly, T₁ and T₂ were upright, T₃ was shallow and inverted, R₄ was present, and T₄ was upright. A blood Wassermann test was negative.

Following this short illness she went to Florida for several weeks and felt well. A few months later, she became weak and tired and had slight low-back pains with a little gas. On the day before her death she spent a busy day shopping, apparently feeling quite well. She went to bed at 9:00 p.m. after a good supper, slept quietly until midnight when she suddenly awoke and complained of severe pain in the mid-upper back and chest. She became extremely orthopneic and dyspneic. On the arrival of her physician a few minutes later she was sitting up in bed, breathing rapidly (40 to 50 respirations per minute). Her pulse was 140 and weak. She was wild-eyed, and there was an ashen cyanosis, with cold sweat. The peripheral veins were not distended. The heart sounds were distant but clear. There were no murmurs. The lungs were clear throughout, there were no rales even at the extreme bases. The abdomen was negative. The patient was given 1/4 gr. of morphine sulfate and 1/150 gr. of atropine sulfate. Although rapid respirations persisted she soon became unconscious. At about 1 a.m. the radial pulse became imperceptible and the blood pressure could not be measured. Oxygen therapy was given for an hour. An electrocardiogram showed a ventricular and auricular rate of about 130 with slight left-axis deviation, an upright T₁ and T₂ and an inverted T₃, there was a PR interval of 0.15 sec., and a slightly elevated ST₁, ST₂ and ST₃, with low voltage. The patient was given Coramin and caffeine and sodium benzoate but expired about two and a half hours after the onset of the attack.

DIFFERENTIAL DIAGNOSIS

DR. F. DENNETTE ADAMS. There is nothing in the record of the first episode to influence one to alter the diagnosis made by the patient's physician of mild respiratory infection. Nervousness, vomiting and a slight inequality of the patellar reflexes occurring in a patient of seventy-eight apparently put the physician on his guard for a

mild cerebral vascular accident. But he obviously found no conclusive signs. Without at least a Babinski sign on one side, demonstrable weakness of a muscle group or some other neurologic sign, an attack of mental confusion or other indication of cerebral insult, slight thrombosis or hemorrhage would have to be dismissed, and the inequality of the patellar reflexes disregarded. Nervousness, in my experience, is to be expected in any old person who is ill. Such patients are always apprehensive. The systolic murmur over the precordium is also relatively unimportant. Basal systolic murmurs due to dilatation of the aorta and apical systolic murmurs due to relative mitral insufficiency are common in the aged.

Examination two months later contributed nothing of importance. Nervousness was still present, and hence not due, as we supposed earlier, to the acute illness alone. The history does not indicate whether there were any disturbing influences in the home environment or elsewhere to account for this symptom.

At the time of the third examination she had easy fatigability, occasional dyspnea and orthopnea. The last two one could assume were signs of beginning myocardial insufficiency. The heart was not large to percussion, but the measurements were perhaps not too accurate, for we note further along in the record that the lungs were hyperresonant. If they were hyperresonant fifteen months later they were probably hyperresonant at the time of this examination although no mention is made of the fact. Further evidence of beginning left ventricular failure is provided by the accentuation of the pulmonary second sound and the lowering of the diastolic pressure from 95—which was reported eighteen months earlier—to 80.

Fifteen months later, at the age of eighty-one the patient developed a pain in the lower ribs which lasted for six days following an attack of "grippe." One is always suspicious of a diagnosis of "grippe" and since here it is in quotation marks, one wonders whether it was made by the patient and not by her physician. Such lay terms as "grippe," "cold" and "gas" often confuse the issue for the doctor unless he is able by careful questioning to get a much clearer idea of just what the patient is attempting to describe. If she actually had a respiratory infection one might be justified in attributing the pain in the lower ribs to acute pleuritis occurring with or without a mild attack of pneumonia. Such a supposition would be more tenable if a relation between pain and respiratory movements had been established. Herpes zoster hardly requires consider-

ation, the typical eruption should certainly be present six days after the onset. There is no mention of restriction of motion or pain on movements of the trunk which might suggest muscular strain or arthritis of the spine as a cause of this discomfort. When pain of this type occurs and the more usual causes are not demonstrable, one must always think of the possibility of pressure or root pain. I am willing to wager that it was because of this possibility that the patient's physician had her x-rayed so promptly. Or perhaps he was confused as he justifiably might have been by the pulmonary signs—slight dullness and diminution of breath sounds in the left scapular region. These are not the signs of pneumonic consolidation or pressure atelectasis. Bronchial breathing or at least bronchovesicular breathing would be expected with either of these disorders. A localized area of fluid too, would be more likely to cause diminished bronchial or bronchovesicular breathing than it would diminished vesicular breathing. The most tenable explanation of these signs, it seems to me is that pressure on a bronchus prevented aeration of a small area of the lung. Yet, not enough lung tissue was affected to cause total absence of sounds because of the presence of unaffected lung surrounding the involved area. X-ray films demonstrated a large mass which must have been tumor, aneurysm or perhaps an encapsulated collection of fluid. At this point I shall ask Dr. Holmes to discuss the x-ray film, although I wonder whether without lateral plates and the benefit of fluoroscopy he will be able to differentiate the various possible causes of the shadow.

DR. GEORGE W. HOLMES: There is an obvious mass in this region. It is round not lobulated. It does not displace the heart or mediastinum. It may to some extent press on the bronchus because there is not much air in the lower part of the chest. The diaphragm is a little elevated high on both sides. The heart shadow, so far as I can make out is slightly enlarged, with the left ventricle more prominent than normal. It would make me suspect slight hypertrophy of the left side of the heart—very little though. I cannot see any evidence of calcification in the walls of this mass. I do not know that I would put much weight on a film like that. What we should like to have is a fluoroscopic observation and films taken with the Bucky diaphragm to give us detail and films taken in the oblique and lateral views. I presume this patient was too sick to have that done. Such a mass as that with the evidence I have here could be either a tumor or a very tortuous aorta. I do not believe it is a tortuous aorta because it is a little larger than

we should be likely to see, and it shows some evidence of pressure on the bronchus, which would not be produced by a dilated aorta. I think it is definitely a tumor. It is in the region of the descending loop of the thoracic aorta.

DR ADAMS: The electrocardiographic report seems to throw very little light on the situation. I am sure Dr. White, since he is here, will give us the benefit of his interpretation of the tracing.

DR PAUL D. WHITE: There is not a great deal out of the way in this first record. There are minor variations from the normal, perhaps a little more left-axis deviation than usual but close to the borderline. There is nothing indicating an acute process in the heart in the first record, nor in the last record. There is little difference between them. There is a statement that there was low voltage, but the voltage is actually just within normal limits and does not indicate any serious process. In other words these are fairly good records for a woman eighty-one years old.

DR ADAMS: Following this illness the patient went to Florida. I see no reason why she should have been prevented from so doing. Certainly with a mass of this size, no matter what it was, there was very little in the way of treatment to be offered, especially in a person of her age. Her condition remained essentially unchanged for a few months except for weakness, easy fatigability and low-back pain, until the final episode which occurred suddenly.

In the middle of the night something happened, and within a few hours she was dead. Of what did she die? And what is the relation of the mass to death? Should one hook them together? The usual medical causes of death occurring within an hour or so are cardiac failure, pulmonary embolism, coronary thrombosis and cerebral hemorrhage. The last named may be promptly excluded without comment. If the patient had had sudden left ventricular failure she would certainly have had, during the subsequent two hours of her life, the signs of acute pulmonary edema, rales in the chest and bloody sputum. If she had had right ventricular failure there would have been more cyanosis and distention of the cervical veins. Furthermore, we have no reason to suspect either of these in a person previously well and without any appreciable degree of heart disease. With extensive pulmonary embolism, too, there would have been more cyanosis and distention of the cervical veins, and there is no reason to presuppose a source for an embolus. Coronary disease is somewhat more difficult to exclude but it seems unlikely because of the severity of the pain in the back, which is rare with coronary thrombosis,

and because, if it took her two hours to die following an attack of coronary thrombosis, some of the signs of heart failure just discussed would have developed. Added evidence that the coronaries were not involved is provided by the electrocardiogram, although electrocardiographic changes might not occur as early as two hours after the onset of such an episode.

DR WHITE: She was very sick, I think we should have expected more evidence in the electrocardiogram if acute coronary thrombosis were responsible for such a grave condition.

DR ADAMS: It is necessary, therefore, to find some other cause of this sudden demise, and naturally one turns to the mass and quite logically wonders whether it was responsible. The mass must have been tumor or aneurysm. I fail to see how a benign tumor could account for the terminal picture. Such a tumor, by pressure on the trachea, might conceivably cause sudden death, but lesser attacks of respiratory distress should have preceded the final attack, and the patient obviously did not die of suffocation. A malignant tumor would probably have given more signs previous to the terminal episode, such as harrasing cough, bloody sputum or, if the apex of the lung were involved, Horner's syndrome. One would also expect more evidence of systemic disease, such as loss of weight, anemia or even greater weakness. Furthermore, a malignant tumor as large as this one would probably show, by roentgenogram, extension of the process into the right side of the chest.

If we exclude tumor — and I think we have done so — then we are forced to the conclusion that this patient had an aneurysm and died of rupture. The clinical picture of the terminal event is consistent with this diagnosis. Sudden pain in the back suggests a perforation. The ashen cyanosis, cold sweat, weakening of the pulse and elevation of its rate are typical of circulatory collapse or hemorrhage. If she had aneurysm, what kind of aneurysm was it? There is no evidence of syphilis; the patient was old for a syphilitic aneurysm, and the Wassermann reaction was negative. The latter does not exclude the disease, although it is strong evidence against it. A negative Hinton test would be even stronger evidence, for this test is rarely negative in the presence of cardiovascular syphilis. Could it have been a dissecting aneurysm? It could have been, but usually with dissecting aneurysm one finds pain gradually extending farther and farther down the back, and often pain in the arms produced by the involvement of the subclavian arteries. Moreover, in my experience, dissecting aneurysm occurs only in patients with hypertension. Now, having already ex-

cluded dissecting aneurysm and having excluded syphilitic aneurysm I am forced into the unhappy position of having to make a diagnosis of sacular aneurysm due to arteriosclerosis. Can arteriosclerosis cause sacular aneurysm? Yes it can although very rarely. I have had in my own practice one case of sacular aneurysm due to arteriosclerosis, but this was in the abdominal aorta. It was proved at postmortem examination. I personally have never seen a sacular aneurysm in the chest due to arteriosclerosis, but if it can occur below the diaphragm I fail to see why it can not occur above. I am by no means unaware of the fact that I am treading on thin ice in making a diagnosis of such a rare disorder, but I believe nonetheless, that this patient had a sacular aneurysm secondary to arteriosclerosis and that rupture of the aneurysm with resultant hemorrhage was the immediate cause of death. Ruptured aneurysm due to syphilis would be my second choice.

DR. TRACY B. MALLORY: Does anyone desire to disagree with Dr. Adams?

DR. J. H. MEANS: I should like to ask Dr. Holmes if the intrathoracic mass could have been a goiter?

DR. HOLMES: I suppose it is a possibility, but a very unlikely one.

DR. MEANS: Some large intrathoracic goiters stick down in a general way, more or less as this mass does. Also may I ask, could it have been an aneurysm of the heart?

DR. HOLMES: No.

DR. MEANS: I am interested in what this patient's condition might have been before the terminal episode. We are told that she had weakness and nervousness which Dr. Adams was inclined to dismiss. I am not certain they should be dismissed. When in an elderly person, they are combined with tachycardia, wide pulse pressure and symptoms suggesting low-grade cardiac insufficiency, they suggest thyrotoxicosis. I should like to know whether she had ever had digitalis or iodine, and, if so, what effect it had on her.

DR. HENRY D. STEBBINS: She had never had either.

DR. ADAMS: I discounted the weakness and nervousness, Dr. Means, because it seems to me that a patient of this age would almost be expected to have both.

DR. CHESTER M. JONES: When was the x-ray film taken in relation to pain in the back?

DR. STEBBINS: It was taken four months and three weeks before the attack of pain.

DR. JONES: The death suggests hemorrhage.

DR. MALLORY: I should like to hear a surgical opinion.

DR. EDWARD D. CHURCHILL: Because of the statement on the day before death that she felt well, spent a busy day shopping and ate a good supper and went to bed, I am inclined to agree with Dr. Adams. It would take something abrupt to kill a person that quickly. I think of hemorrhage from a dissecting aneurysm.

A PHYSICIAN: I should like to ask Dr. Adams whether the possibility of thoracic tumor with erosion of a vessel followed by hemorrhage should be considered.

DR. ADAMS: Yes that is a possibility. My experience with intrathoracic tumors is limited, but as I pointed out earlier I should expect the patient to have had cough, bloody sputum or by x-ray some evidence of tumor in the right side of the chest as well as the left. A fluoroscopic examination showing the presence or absence of pulsation would have been helpful, although not conclusive, for with tumor pulsation can be transmitted from the aorta and cause a mistaken diagnosis of aneurysm.

DR. MALLORY: Dr. Stebbins, you had the care of this patient. Have you anything to add?

DR. STEBBINS: No. I know the answer so probably I had better not add anything, but I should be glad to answer any questions.

DR. CHURCHILL: What was your diagnosis?

DR. STEBBINS: Mine was the same as that of Dr. Adams and Dr. White, who also saw the patient.

DR. WHITE: I saw her during the last ten minutes of her life and have nothing to add. It certainly was striking as Dr. Churchill has said, that she had been well and very active that day and that she suddenly became acutely ill and died so quickly. We suspected that death was due to rupture of an aortic aneurysm and not to heart failure or coronary disease.

DR. MEANS: The x-ray film was taken some time before death. If she died of ruptured aneurysm the story suggests dissecting aneurysm more than it does syphilitic aneurysm. The x-ray picture is certainly not that of dissecting aneurysm.

DR. HOLMES: I should be inclined to agree with that.

DR. MEANS: I think she could have had a dissecting aneurysm. However, Dr. Adams was talking along the lines of syphilis, which I think is unlikely.

DR. ADAMS: You must have misunderstood me, Dr. Means. My first diagnosis was arteriosclerotic sacular aneurysm. Syphilis is a possibility, but unlikely.

DR. CHURCHILL: It is rare to get a dissecting aneurysm in the presence of hypertension.

DR ARTHUR W ALLEN I think she lived too long for a patient with a ruptured saccular aneurysm—two and a half hours

DR ADAMS The patient whom I mentioned with abdominal aneurysm lived for forty-eight hours after the rupture

CLINICAL DIAGNOSIS

Ruptured dissecting aneurysm of aorta

DR ADAMS'S DIAGNOSIS

Arteriosclerotic saccular aneurysm, with rupture

ANATOMICAL DIAGNOSES

Arteriosclerotic aneurysms of aorta, multiple, with rupture of one into right pleural cavity

Aneurysm of the left common iliac artery, arteriosclerotic

Hemothorax, right

Pulmonary atelectasis, compression of left lower lobe

Arteriosclerosis, marked, aortic, slight, coronary and renal

Operative scars simple mastectomy, right, appendectomy

PATHOLOGICAL DISCUSSION

DR MALLORY At postmortem the right pleural cavity contained 2000 cc of blood. On tracking down the source of the hemorrhage a large, saccular intrathoracic aneurysm of the descending aorta was found. There was another smaller thoracic aneurysm and a large abdominal one, and there was a fourth aneurysm of one of the iliac arteries. I think that the multiplicity of aneurysms in this case might have been determined on physical examination. Perhaps both the one in the iliac artery and the one in the abdominal aorta could have been felt if examination had been made specifically for that possibility. She was obese, however, and it might not have been possible. The aneurysms showed very calcareous walls, with no evidence of syphilitic aortitis, and are definitely of the arteriosclerotic type. It is rather characteristic of such sclerotic aneurysms to appear in the abdominal rather than the thoracic aorta, but they can occur in either place. There was no histological evidence of syphilis, and I think we can accept the serological test as having been verified.

DR WHITE It is the first case of the sort I have ever seen, and I wonder what your experience has been here with arteriosclerotic aneurysm.

DR MALLORY We have seen very few in the thoracic aorta, but they are not infrequent in the

abdominal portion. Two other favorite locations are the iliac and the popliteal arteries.

DR WHITE How were the coronaries?

DR MALLORY There was no marked degree of atheroma and no narrowing anywhere.

DR WHITE It seems to me that an arteriosclerotic aneurysm is a condition not well recognized in the literature, at least so far as the thoracic aorta is concerned. Our cases ought to be collected and reported.

CASE 25522

PRESENTATION OF CASE

A twenty-eight-year-old Polish grocery clerk entered the hospital because of pain and swelling of the right elbow.

Twelve months before admission the patient wrenched his right elbow while cranking an automobile. The soreness which resulted disappeared without treatment, and except for slight aching, he was well until about six weeks before entry when the joint "snapped" during an act of normal movement. It became hot, red, swollen and tender. He noted a scraping feeling on moving the joint, and there was limitation of both flexion and extension. His physician took x-ray films of the part and aspirated fluid from the joint but was unable to make a definite diagnosis. Following aspiration the pain diminished for a while, but soon returned. He noticed no other symptoms.

Physical examination revealed a very apprehensive, hyperactive, co-operative young man in apparent acute distress. The left elbow was slightly swollen but not hot, there was fullness over the head of the radius. The right elbow measured 26 cm in circumference, the left 23.8 cm. Motions were limited on the right as follows: supination, 20°, extension, 40°, flexion, 110°, pronation, normal. Motions on the left were normal. On pronation and supination there was an occasional grating in the elbow, with tenderness over the radial head, olecranon and medial epicondyle. The heart, lungs and remainder of the examination were negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,450,000 with 15.3 gm hemoglobin (photoelectric cell method), and a white-cell count of 11,500 with 63 per cent polymorphonuclears. The urine examination and blood Hinton tests were negative. The spinal-fluid protein was 52 mg per 100 cc, the gold-sol and Wassermann tests were negative.

On the sixth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. EDWIN F. CAVE In discussing this case, it seems important to decide whether the disease originated in the joint itself, in the bursa or bursas about the joint or in the ends of the bones that go to make up the joint. It impresses me as being a case of disease of the joint itself, a case of mild trauma with superimposed infection of some nature. Several possibilities come to one's mind. Here is a young man of twenty-eight, apparently a husky fellow who did relatively heavy work and subjected all his joints to strenuous activity. It is, therefore, not unlikely that there has been sufficient trauma to the elbow joint either by excessive strain or by direct blow, to result in aseptic necrosis of the joint cartilage, and finally the development of an osteochondritis. We do know that such a condition occurs in the elbow second in frequency only to that of the knee joint. But, this alone will not explain the findings in the particular joint under discussion. If we are dealing with osteochondritis there must also be superimposed infection of some nature. The essentially normal blood, — except for slight elevation of the white-cell count, — the normal temperature and pulse are against any virulent infection. The duration of six weeks is also against that. The fact that he had mild symptoms for a period of ten and a half months before the acute process developed suggests that there was latent infection present during this time. I do not believe that this is a case of infectious arthritis, and tumors of bone in this region are rare. Ewing's tumor does not occur in such close proximity to joints, and a normal temperature is also against this diagnosis. Osteomyelitis of the humerus, ulna or radius in this region is a remote possibility and could account for the joint swelling, but again this condition is rare in this region, and probably could be ruled out by the blood findings, normal temperature and pulse. Syphilis may be discarded because of the negative blood Hinton, spinal fluid Wassermann and gold-sol curve.

The two possibilities which impress me as being most likely are Neisserian infection of the elbow joint and tuberculosis. The duration of symptoms and the apparent acuteness of the joint are not inconsistent with the diagnosis of gonococcal infection. If this is the diagnosis, I am certain that the infection had been present only for six

weeks, and had nothing to do with the mild symptoms in the joint during the past year. I do not believe however, it could be due to the gonococcus because of the relatively low white-cell and polymorphonuclear counts and the normal temperature.

I think it could perfectly well be due to tuberculosis and that is my diagnosis. His age and the duration of symptoms are consistent with this diagnosis. We should like to know what x-ray films of the joint showed what the tuberculin test was and whether any lesion was demonstrable in the chest plate. The slight elevation in white count and the polymorphonuclear count of only 63 per cent, hence a relative lymphocytosis, furnish confirmatory evidence for the diagnosis of tuberculosis.

The swelling of the opposite elbow is difficult to explain, but this may also be due to tuberculosis, because we know that in a series of 215 cases of spinal tuberculosis in this hospital, between one fourth and one third had more than one joint involved. This statement also holds true in a group of 90 children at the New England Peabody Home for Crippled Children. It may be that in the left elbow we are dealing with a synovial type of tuberculosis without demonstrable lesion by x-ray.

CLINICAL DIAGNOSIS

Traumatic arthritis, ? loose bodies

DR. CAVE'S DIAGNOSIS

Tuberculous arthritis of the right elbow

ANATOMICAL DIAGNOSIS

Tuberculous arthritis of the right elbow

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY The joint was explored and the surgeon found that the joint space was filled with so-called "rice bodies" and, on further exploration that there was a sizable cavity in the olecranon and another in the coronoid process. The joint cartilage was eroded in several spots, and the entire picture was quite typical of tuberculosis of the joint, the diagnosis was confirmed by microscopical examination. A fusion was performed, and the patient had a fairly quick and satisfactory convalescence.

The New England Journal of Medicine

Formerly the
Boston Medical and Surgical Journal
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE
ON PUBLICATIONS

Official Organ of
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THE NEW HAMPSHIRE MEDICAL SOCIETY
THE VERMONT STATE MEDICAL SOCIETY

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SUBSCRIPTION TERMS \$6.00 per year in advance, postage paid for the United States Canada \$7.04 per year \$8.52 per year for all foreign countries belonging to the Postal Union.

MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine* 8 Fenway Boston Massachusetts

—AND A HAPPY NEW YEAR

WE have come to think of our New Year greeting, perhaps, too much in reference to the day, and not enough in reference to the year, as was undoubtedly its original intention. Christmas is our day of festival, a day with double meaning, derived from a spiritual satisfaction at the birth of our accepted religious leader and from an older, more sensuous satisfaction at the beginning of the return of the sun to northern latitudes and the consequent lengthening of the days.

It is appropriate that, as the shortest day is passed and the hours of sunlight begin to increase, we should reckon our new year as beginning. With and between the two holidays we

have our one Christian festival season marking the beginning of a new era in man's relations to man and the start of a new year in which to put these relations into effect. After the Christmas-New Year holidays we have our winter, but after them we have also the sun's northward journey to watch and to mark off on our calendars, until the coming in of spring.

Our "Happy New Year," then, connotes more than a day on which to express a greeting and to congratulate ourselves and each other on living in a hemisphere at peace and in relative prosperity. It is the introduction to another year—a new cycle of seasons through which we strive to live as successfully, as efficiently and as happily as our inner resources permit.

One of the happy functions of New Year's Day is to afford an opportunity of brushing up on our good resolutions for the incoming year. This is sometimes a source of cynicism or mirth because resolutions so seldom last throughout the twelve months. This does not detract from their value. A good suit also needs to be brushed and pressed, and shoes to be polished. The more use they are to us, the more they need these services. The refreshing of resolutions does not mean that they are for show only, but that they have merit. The new year offers a particularly appropriate opportunity for setting our individual houses in order.

A NEW LIBRARY OF MEDICAL HISTORY FOR YALE

A LIBRARY devoted to the history of medicine has recently been established at Yale University School of Medicine. A building is about to be erected, which will contain, in addition to the material already available, three important collections of books. The first is that of the late Dr. Harvey Cushing. This collection, one of the most important private medical libraries in the world, is particularly rich in material relating to Vesalius.

and the pre Vesalius anatomists. In addition, there are many books on surgery, including a superb collection of volumes by Pare and hundreds of items on medical education, schools, biographies, histories and material of a similar character. Secondly, there is to be added to this the library of Dr John F. Fulton, Sterling Professor of Physiology, Yale University. His collection of books is also notable, for it contains the fundamental physiological treatises of the past, as well as a large number of purely literary contributions by physicians and scientists. Fortunately there is little duplication in the two collections. Finally, word has been received from Switzerland that the library of Dr Arnold C. Klebs, an old friend of Dr Cushing, who has lived in Switzerland for many years, but who is an American citizen, will be added to the two collections mentioned above. Dr Klebs's collection, again, is unique and different from that made either by Dr Cushing or by Dr Fulton. His primary interest has been in the printing of early books, especially those issued in the fifteenth century that were of a medical or scientific nature. His library consists largely of the apparatus useful to a medical or scientific bibliographer. It is not rich in early printed books themselves, but is a most unusual collection of books about books, printers, type, paper and other aspects of the printing trade before 1500.

To house these collections a new wing is being added to the Sterling Hall of Medicine, with room for about 400,000 volumes. In one part of the building will be the historical collections noted above and in another a working library for the medical school. The building, on the medical school grounds and adjacent to the New Haven Hospital will form an integral part of the Yale medical unit.

Dr Cushing's collection of books is so important that its acceptance by Yale University is an epoch-making step. New Haven will become a center for students of medical history such as has not been developed elsewhere, except possibly in the home of the greatest collection of all the Army

Medical Library in Washington. The new library will form, moreover, a link in a chain of medical libraries extending from Montreal through Boston, New Haven, New York, Philadelphia and Baltimore to Washington. By traveling this path a scholar of medical history will have available to him the most significant books dealing with medicine in the past. The Yale link in the chain will be by no means a weak one, for the collections given by Cushing, Fulton and Klebs form a nexus of great strength. Yale University is to be congratulated on visualizing the importance of these collections and seeing that they are suitably housed.

OBITUARY

SUMNER MEAD ROBERTS

1898-1939

Sumner M. Roberts was instantly killed in an automobile accident November 19, 1939.

He was born on January 25, 1898 in Dedham and attended the public schools there as a child. His family moved to Chestnut Hill when he was about ten and he then entered the Country Day School where he prepared for college. At the latter he was a member of the football, track and baseball teams and of the student council. Then he went West for a year to the Mesa School at Phoenix, Arizona. During his first year at Harvard College, which he entered at the age of eighteen, he was on the freshman football and baseball squads. When the War came on and called him, he elected to enter the naval service. For preliminary training he shipped as a member of the crew of a South American cargo boat, then entered the Naval Reserve and went to school at Charlestown. He was commissioned as ensign in the United States Navy but never went to sea. He was discharged soon after the Armistice and re-entered Harvard College. During the following summer he went to Hawaii with Charles Thorndike to work with Dr. Thomas A. Jagger, who was engaged in the study of the crater of the volcano Kilauea.

He was graduated from Harvard College in 1921, with a war degree of A.B., having taken special courses in zoology and biology. After four years at the Harvard Medical School, he received an appointment as surgical intern at the New

York Hospital, working under Dr Eugene H Pool. He then took a two year postgraduate course in orthopedic surgery under the auspices of the Harvard Medical School, the Children's Hospital and the Massachusetts General Hospital. On completing his medical training he entered private practice and became associated with Drs Robert B Osgood, Philip D Wilson and Francis C Hall at 372 Marlborough Street.

He was assistant visiting orthopedic surgeon at the Massachusetts General Hospital, consulting surgeon at the Robert Breck Brigham Hospital and assistant in orthopedic surgery at the Harvard Medical School. He was a member of the American Medical Association, Massachusetts Medical Society, American College of Surgeons, Aesculapian Club, American Academy of Orthopaedic Surgeons and American Orthopaedic Association. He was president of the Boston Orthopaedic Club at the time of his death.

He was married on December 27, 1927, to Elizabeth Converse, the daughter of the eminent musician and composer, Frederick S Converse. He is survived by his widow and three children.

The swift communication of the news of his untimely death by word of mouth from friend to friend and the immediate sense of grief which fell on all testify only too well to the affection and respect which his personality had engendered. He was straightforward and sincere. Courage and simplicity, which love of the outdoors seems to breed, were his in abundant measure. He found a pleasure in the lonely wood and at the shore which gave him peace of mind and tranquillity, undisturbed by trivial things.

Professionally he received an excellent training and then chose orthopedic surgery as his field. The treatment of fractures and the rehabilitation of the severely crippled arthritic patient were problems which particularly interested him, and his contributions to the knowledge of these subjects are of lasting merit. His patients, including those on the hospital wards, regarded him with trust, and each was rewarded by a well-planned and dexterously executed attempt at cure or amelioration of his afflictions.

His modesty and reserve prevented him from becoming a favorite of the crowds, but few physicians can number more sincere friends than he among their colleagues. At the zenith of his ability, but before the great honors which were rightly his had sought him out, his life was taken. We have lost a great physician, even as his family has lost an exemplary husband and father.

J S B

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SECTION OF OBSTETRICS AND GYNECOLOGY*

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FATAL PUERPERAL SEPSIS FOLLOWING FORCEPS DELIVERY

Mrs B A, a twenty-eight-year-old woman, was admitted to the hospital on March 24, 1926, complaining of acute severe abdominal distention with copious black vomitus. A para I, she had been delivered at home with forceps on March 21. Vomiting, dehydration and abdominal distention had followed the delivery. The patient had also had continuous abdominal pain, which had begun on March 23. The family history and past history were not obtained.

On entry the temperature was 101.6°F, the pulse 136, and the respirations 40. The patient was toxic, dehydrated and febrile, with a markedly distended, extremely tender, spastic abdomen, especially in the hypogastrium. The heart was not enlarged, there were no murmurs. The lungs were clear and resonant, there were no rales. A rectal examination was negative. The white-blood-cell count was 3800, and the urine showed pus and casts.

She was given immediate gastric lavage, subpectoral fluids, enemas, rectal fluids, posterior pituitary extract, and flaxseed poultices to the abdomen. The patient's course was progressively downhill, and she became more and more toxic, irrational and distended. Just before she expired on March 25 the temperature was 105.2°F, the pulse 160, and the respirations 36.

Comment. The case of this patient, who had vomiting, abdominal distention and fever thirty-six hours after delivery, suggests that the uterus had been partially ruptured in the lower segment. The abdominal symptoms of peritonitis occurred much more quickly than they would have if the infection were limited to the uterus. No blood culture or uterine culture was taken. The patient was apparently a very sick woman at the time of entry, and her best chance of recovery lay in following strict conservatism.

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

DEATHS

MEAD—GEORGE N MEAD M.D., of Winchester died December 14. He was in his eighty first year.

Born in Concord, New Hampshire, he graduated from Phillips Exeter Academy and attended Harvard University. He received his degree from Harvard Medical School in 1886 and interned at the Massachusetts General Hospital. He practiced for a short time in Everett and then joined the staff of the Winchester Hospital. Dr Mead retired from active practice in 1929.

He was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow and a son survive him.

SCHMIDT—RICHARD D SCHMIDT M.D., of Dorchester died December 18. He was in his sixty ninth year.

Born to Roxbury he attended public schools in Boston and Brooklyn New York, and became a registered pharmacist before entering medical school. He received his degree from Tufts College Medical School in 1904.

Dr Schmidt was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow a son and a brother Dr Frederick Schmidt survive him.

MISCELLANY

ANNOUNCEMENT OF THE FRANCIS AMORY SEPTENNIAL PRIZE OF THE AMERICAN ACADEMY OF ARTS AND SCIENCES UNDER THE WILL OF FRANCIS AMORY

In compliance with the provisions of the will of the late Francis Amory The American Academy of Arts and Sciences as trustees of a fund given by the testator announces a prize to be known as the Francis Amory Septennial Prize to be awarded for conspicuously meritorious work performed during the immediately preceding septennial period through experiment study or otherwise, in the treatment and cure of disease and derangement of the human sexual generative organs in general and more especially for the cure, prevention or relief of the retention of urine, cystitis, prostatitis and so forth. While the donor wished especially to reward the discovery of any new method of treatment, he expressly authorized that the prize might be given to any author who might have contributed any theoretical or practical treatise of extraordinary or exceptional value and merit on the anatomy of said organs or the treatment of their diseases.

If there shall appear work of a quality to warrant it, the first award will be made in 1940. The total amount will exceed \$10,000 which may be divided at the discretion of the Academy among several nominees. While formal nominations are not expected and no essays or treatises in direct competition for the prize are desired the Committee on the Francis Amory Septennial Prize invites suggestions looking toward the wise performance of its duty. Communications on this subject should reach the committee not later than May 15 1940 and should be addressed in care of the American Academy of Arts and Sciences 28 Newbury Street, Boston. The members of the committee are: Dr Roger I Lee, chairman Dr Walter B. Cannon, Dr David Cheever Prof Leigh Hoadley Dr William C. Quinby, Dr Ernest E. Tyzzer and Dr Soma Weiss, secretary.

NOTE

The Committee on Faculty of Middlesex University has announced the appointment of Dr Karl Singer as associate professor of physiology in the School of Medi-

cine. Dr Singer was born in Vienna where he received his medical degree in 1927. He served as acting superintendent of the Kaiser Franz Joseph Hospital and as a member of the Department of Hematology of the University Clinic in Vienna. For ten years he was an associate in applied physiology in the University of Vienna Medical School and research fellow of the Academy of Sciences. He came to Boston last year where he became a research fellow in hematology at the Beth Israel Hospital.

CORRESPONDENCE

A FAIRY TALE

To the Editor

Once upon a time a citizen who had a controlling interest in a successful drug emporium and was philanthropically inclined decided that people needed an extension or alteration of medical services. So, he formed a charitable corporation with his niece and the druggist's son as the salaried agents of the corporation. Then he made an agreement with a doctor who had an office nearby that the niece should collect all fees paid to the doctor retain 20 per cent for operation of the charitable corporation and return 80 per cent to the doctor. The druggist, who received no salary from the corporation suggested that people go to see the doctor because he was well equipped with all kinds of stethoscopes cystoscopes, proctoscopes, electrocardiographs and x-ray apparatus and had young men do work which he himself did not wish to do or did not feel qualified to do. The charitable corporation soon suggested that tickets for medical care be issued and sold in blocks at reduced prices and a little later that tickets be sold annually to cover all medical services. The druggist continued to urge people to go to the doctor whose office was near the store. By the same token the drug emporium was near the doctor's office. The druggist, the citizen and their families spoke to friends about the wonderful new plan and urged that they all leave their present doctors and join up. The citizen was even invited to speak before groups in churches to mercantile associations and in stores where there were considerable numbers of employees. (Of course, the doctor who was under contract with the charitable corporation never himself solicited any body to come to him.)

This is the first installment of the fairy tale. Perhaps some other member or members of the Massachusetts Medical Society would write the second installment, telling what happened to the quality of medical practice given the people of the community during the succeeding ten or twenty years.

DAVID HALBERSTADEN M.D.

3 Conway Street,
Roslindale, Massachusetts.

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor. In addition to the articles enumerated in our letter of November 2 the following have been accepted.

International Vitamin Corporation

I V C. Ascorbic Acid Tablets

I V C. Thiamin Chloride Crystalline Tablets, 0.5 mg.

I V C Thiamin Chloride Crystalline Tablets, 10 mg
I V C Thiamin Chloride Crystalline Tablets, 33 mg

Mead Johnson & Co

Mead's Mineral Oil with Malt Syrup

New York Quinine and Chemical Works

Nicotinic Acid—N Y Q

Parke, Davis & Co

Vitamin K in Oil

Capsules Vitamin K in Oil

PAUL NICHOLAS LEECH, *Secretary*

535 North Dearborn Street,
Chicago, Illinois

REPORTS OF MEETINGS

PALMER MEMORIAL HOSPITAL

A symposium on cancer of the tongue was held on Tuesday, June 13, at the Palmer Memorial Hospital, with Dr Leland S McKittrick presiding. The discussion was conducted by the staffs of the Massachusetts General, Huntington Memorial, Pondville and Palmer Memorial hospitals.

The first speaker, Dr Ira T Nathanson, of the Huntington Memorial Hospital, reported on 387 primary cases of cancer of the tongue treated at that institution between 1922 and 1936. Of these only about 35 per cent were in Group 1A, that is, without palpable nodes of any sort on admission. Cure of the local lesion was accomplished in 39 per cent of the Group 1A cases and in 16 per cent of the Group 1B cases. Dr Nathanson found duration of the lesion to be insignificant but size and position on the tongue of great prognostic import in local cures for both groups.

In the development of metastatic nodes in the neck, the grade and size of the primary lesion played an important role, and these same factors were not significant in affecting the curability of the nodes. As in the primary lesion, duration of the disease was not a factor. Size of the nodes could not be taken as a positive criterion of malignancy, for 76 per cent of those which were 1 cm or less in diameter were eventually malignant. When nodes were more than 1 cm in diameter, over 95 per cent were malignant.

Of those subjected to radical surgery, there was a 25 per cent cure of those with positive cervical nodes. Cures of three years or more were obtained in 31 per cent of the Group 1A cases and in 8 per cent of those in Group 1B, with a total salvage for all cases of 15 per cent.

Dr Nathanson concluded that operable and accessible lesions seemed to be offered the best chance of local cure by surgery, but admitted that insufficient treatment had been given in comparable irradiated cases. If no nodes were palpable in the neck, or were palpable but less than 1 cm in diameter, and if the primary lesion was small and of low grade malignancy, one was justified in careful surveillance of the nodes since their curability was not influenced by their palpability. However, when the nodes were 1 cm or greater in diameter, especially if the primary lesion was higher than Grade I and larger than 1 cm, rigorous treatment was to be directed toward the nodes. Management of the lymph nodes, however, should not be undertaken until the primary lesion has been cured or brought under control.

Dr Roy E. Mabrey presented 106 cases of cancer of the tongue treated from 1927 to 1935 at the Massachusetts

General Hospital. Pathological study of cervical nodes removed surgically indicated that large primary lesions were prone to give rise to positive nodes, and that large nodes were likely to be positive. Some palpable nodes, however, were negative at operation, whereas some nonpalpable nodes showed evidence of metastasis.

Cure of the local lesion resulted more often in cases with anterior lesions, and surgery gave the best therapeutic results, as at the Huntington Memorial Hospital. Three year cures in Group 1A amounted to 20 per cent, and in Group 1B to 0.6 per cent, with a total salvage of 11 per cent for the entire group. Cures were obtained in 39 per cent of those treated surgically, the operative mortality was 11 per cent.

Dr Clifford C Franseen reported the results of 50 cases from the Palmer Memorial Hospital. In regard to possible etiologic factors, leukoplakia was mentioned as a definite precursor in 20 per cent, syphilis in 18 per cent, and poor teeth in 24 per cent of the cases, but Dr Franseen ventured that a greater number would be found to have leukoplakia if the condition were sought and its presence recorded.

Of those treated by surgery alone 29 per cent were cured for three years or more, and there was a 15 per cent operative mortality. The gross salvage on all cases was 14 per cent.

Dr Franseen's statistics re-emphasized the lack of correlation between palpability of neck nodes and malignancy, for in only 1 out of 8 cases with palpable nodes were they positive, whereas the nodes were malignant in 3 of 5 cases with prophylactic neck dissections.

Dr Thomas Anglem, representing the Pondville Hospital, reported on 109 primary cases. The grade of malignancy in this series also seemed essentially unimportant in regard to prognosis. Thirty-eight per cent of the Group 1A cases were cured and none of those in Group 1B, with a total salvage of 11 per cent. Cures by surgery were in the same range as in the other series, namely 31 per cent. The operative mortality was 21 per cent. Radiation cures of 25 per cent were by far the best of any group.

Dr Channing C Simmons, chief surgeon of the Huntington Hospital, discussed the papers, pointing out that the end results obtained from the four hospitals were essentially the same. Surgical cases on the whole fared better than those irradiated, even when due consideration was given to operability of the lesions. Lesions situated on the anterior part of the tongue had a better prognosis by either method of treatment, due to their accessibility and lower grade of malignancy. Dr Simmons emphasized that duration was of little consequence, as in breast cancer, for tumors of low malignancy grow slowly and offer just as favorable if not a more favorable outlook than do the rapidly increasing, highly malignant lesions. The speaker said that irradiation undoubtedly offered a better opportunity for palliation in the inoperable lesions but offered statistics to substantiate his faith in the surgical treatment of operable lesions. Thus 83 per cent of the operable cases were cured of the local lesion, and 60 per cent were totally cured. Dr Simmons admitted, however, that a sufficient dosage of irradiation had not been given in most instances, and recommended 3000 to 5000 r externally, in addition to local radium or intraoral x-ray.

In the management of the lymph nodes, their size, consistence and movability should be considered, as well as the general condition of the patient and his ability to tolerate the contemplated procedures. Radical operation, Dr Simmons said, was easier than incomplete neck dis-

section, and all the above surgical mortality figures were given as proof of this statement.

Dr Simmons concluded that the results depended largely on the facilities at hand either a good surgeon and anesthesiologist in the proper environment or a well trained irradiation expert with the proper equipment. For although surgery appeared to offer a better chance for cure in these studies irradiation therapy was rapidly improving and appeared promising.

Dr W Martindale Shedden opened the general discussion with a plea for more and better radiation of cervical metastases on the ground that only 9 per cent of cases were found suitable for radical operation by Duffy of the Memorial Hospital in New York. He stated that better irradiation might conceivably give results comparable to those of surgery.

Dr Ernest M. Daland assured the audience that the outlook was not so disappointing as it appeared for treatment was improving and the reported cases were not from the most recent years, since not enough time had elapsed to evaluate the final results.

Dr George W. Holmes suggested that the high mortality and long delay to treatment reflected the poor selection of cases in clinics which obviously got the worst cases. He stated that surgery had probably attained its peak and that any improvement would have to come from a better selection of cases for surgery and an advance of irradiation technique, which he said was already occurring. He stated that this community was surgically minded due to its better training in that field than in radiology.

Dr Anglem summarized the findings of the four investigators from the various institutions. Cancer of the tongue was considered essentially as two entities those lesions behind the circumvallate papillae which act like pharyngeal lesions and are treated almost exclusively by irradiation and those lesions on the anterior portion of the tongue which can be treated equally well by adequate surgery or competent irradiation, although past statistics favored the former. Inoperable anterior lesions would receive irradiation as high at least as 10,000 to 12,000 r one half being given intraorally.

He divided the management of lymph nodes into that relating to the palpable, non-palpable and inoperable groups. It was considered justifiable with non-palpable nodes or those less than 1 cm. in diameter to observe the neck closely rather than to perform a prophylactic dissection. Nodes 1 cm or larger but movable should be subjected to radical operation only if the patient's general condition is excellent, for the salvage of positive nodes is only 15 or 20 per cent whereas the operative mortality reaches 10 per cent. Dr Anglem advocated that the alternate treatment with x-rays and interstitial radium be used in some of these so-called operable cases. Inoperable nodes should be treated first with x-rays to decrease their size, and then radium should be implanted in the remnants.

Dr Anglem reiterated several times the importance of giving large amounts of radiation early and in concentrated doses, so that the cancer can be cured with a minimum degree of deleterious effect on the tumor bed and surrounding blood supply upon which cure largely depends. He cautioned however against the use of large portals which were responsible for the poor results obtained in former years with large amounts of irradiation.

CONFERENCE ON ENVIRONMENTAL SANITATION

The last in a series of four conferences on environmental sanitation was held at the Department of Public Health Yale University School of Medicine on Thursday December 14. The sessions which were under the auspices of the Department of Public Health in co-operation with the Connecticut State Department of Health the Connecticut Dairy and Milk Inspectors Association and the Connecticut Public Health Association were attended by about forty health officers and sanitary inspectors from all parts of Connecticut. Mr Martin A. Pond instructor in public health directed these conferences.

Among the topics discussed were milk sanitation including inspection of farms and plants, food sanitation, including restaurant and food-manufacturing-establishment inspections, public health law and problems of water supply, housing, sewage disposal and other sanitation activities. Besides representatives of local health departments and the Connecticut State Department of Health experts from the United States Public Health Service, the United States Food and Drug Administration and the New York City Department of Health participated in the meetings.

NOTICES

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday evening January 2, at 8:15.

Dr Abraham Myerson will speak on "Recent Advances in the Treatment of Epilepsy and Schizophrenia."

MAX RITVO M.D., *President*
DAVID B. STEARNS M.D., *Secretary*

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall 9-10 a. m.

MEDICAL CONFERENCE PROGRAM JANUARY FEBRUARY

- Tuesday January 2—Thirty Years Experience in the Treatment of Fractures. Dr John D. Adams.
- Wednesday January 3—Hospital case presentation. Dr S. J. Thannhauser.
- Thursday January 4—Estrogen and Androgen Assay. Indications and Interpretations. Dr N. T. Wertheimer and Dr C. H. Lawrence.
- Friday January 5—The Treatment of Epilepsy by Phenobarbital and Dilantin Sodium and by Various Synergistic Drug Combinations. Dr Benjamin Cohen.
- Saturday January 6—Hospital case presentation. Dr S. J. Thannhauser.
- Tuesday January 9—Certain Hematological Problems. Dr W. Dameshek.
- Wednesday January 10—Hospital case presentation. Dr S. J. Thannhauser.
- Thursday January 11—The Place of Electrocardiography in Clinical Diagnosis. Dr J. M. Faulkner.
- Friday January 12—The Present Day Specific Treatment of Pneumonia. Dr Maxwell Finland.
- Saturday January 13—Hospital case presentation. Dr S. J. Thannhauser.
- Tuesday January 16—Nephritic Clinic. Presentation of cases. Dr R. W. Buck.

Wednesday, January 17—Hospital case presentation Dr S J Thannhauser
 Thursday, January 18—Surgical Case Clinicopathological presentation. Dr H. F. Day
 Friday, January 19—A Discussion of Rheumatic Fever Dr T Duckett Jones
 Saturday, January 20—Hospital case presentation. Dr S J Thannhauser
 Tuesday, January 23—X-Ray Clinic Presentation of cases Dr A Ettinger
 Wednesday, January 24—Hospital case presentation Dr S J Thannhauser
 Thursday, January 25—Otolaryngology Clinic Presentation of cases Dr P E Meltzer
 Friday, January 26—Peritoneoscopy in Diagnosis of Abdominal Tumors Dr W E. Garrey
 Saturday, January 27—Hospital case presentation Dr S J Thannhauser
 Tuesday, January 30—Aneurysm and Rupture of the Ventricle of the Heart. Dr M N Fulton.

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, January 3, from 2 to 4 p.m. Drs William C. Quinby and E. A. Stead will speak on "Hematuria." A clinicopathological conference, conducted by Dr Elliott C. Cutler, will take place from 4 to 5 p.m.

On Thursday, January 4, from 8:30 to 9:30 a.m. there will be at the Children's Hospital, a combined clinic, conducted by Dr William E. Ladd, of the medical, surgical, orthopedic and pediatric services of the Children's Hospital and the Peter Bent Brigham Hospital.

Physicians and students are cordially invited to attend.

ELLIOTT C. CUTLER, M.D., *Secretary*

FAULKNER HOSPITAL

CLINICOPATHOLOGICAL CONFERENCE

The monthly clinicopathological conference of the Faulkner Hospital will be held on Thursday, January 4, at 5:00 p.m. Drs David Halbersleben and G. M. Morrison will discuss cases.

Interested members of the medical profession are invited to attend.

FREE PUBLIC LECTURES

Harvard University has recently announced the subjects and speakers in its course of free public lectures on medical topics that are given each year at the Harvard Medical School. As usual these will be given in the amphitheater of Building D at 4:00 p.m. on Sundays. The schedule is as follows:

January 7 Digestion and Indigestion Dr Chester M. Jones
 January 14 Serious Accidents: What to do and what not to do Dr Charles C. Lund.
 January 21 What About Sulfanilamide? Dr Chester S. Keefer
 January 28 Care of the Complexion. Dr Perry C. Baird, Jr.
 February 4 Facts and Fancies About Heart Disease. Dr Paul D. White.
 February 11 Cancer Dr Grantley W. Taylor
 February 18 The Medical Care of Domestic Pets Dr Gerry B. Schnelle.
 February 25 Sterility (lecture for women only) Dr Donald Macomber
 March 3 Backache. Dr Frank R. Ober

March 10 Health in Middle Age. Dr William B. Breed

CUTTER LECTURES

Dr Ludvig Hektoen, executive director of the National Advisory Cancer Council of the United States Public Health Service, will give the first of a series of two annual Cutter Lectures in Preventive Medicine at the Harvard Medical School on Monday, January 15. He will talk on the general subject of cancer control with special reference to its public health and epidemiological aspects. The second lecture will be given by Dr James B. Murphy, member of the Rockefeller Institute for Medical Research, on Monday, January 22. Dr Murphy will give a critical review of experimental studies in cancer.

Both lectures will be held at 5:00 p.m. in Amphitheater E at the Harvard Medical School. The medical profession, medical and public health students and others interested are invited to attend.

SALEM HOSPITAL PUBLIC HEALTH LECTURES

The Salem Hospital will conduct a series of Sunday afternoon lectures this winter on medical subjects of general public interest. The purpose of these lectures is to afford the layman an opportunity to gain an accurate knowledge of methods for the protection of his health and the prevention of illness.

The lectures will be free to the public and will be held in the auditorium of the Salem Hospital during January and February, at 4:00 p.m.

The program is as follows:

January 7 New Weapons Against Disease. Dr Stuart N. Gardner
 January 14 Abuse of Household Gadgets Dr Walter G. Phippen
 January 21 Infantile Paralysis Dr Edwin D. Reynolds
 January 28 Work and Leisure. Dr William V. McDermott.
 February 4 Anemia and Blood Transfusions Dr J. Robert Shaughnessy
 February 11 Health of the School Child Dr Charles H. Hogan
 February 18 Obstetrical Facts and Fancies Dr Benjamin D. Cornwall
 February 27 Your Eyes Dr Henry G. Carroll

NORFOLK DISTRICT MEDICAL SOCIETY

A special meeting of the councilors of the Norfolk District Medical Society will be held in Sprague Hall in the Boston Medical Library, Wednesday, January 3, at 12 noon.

The call of this meeting is on petition of the West Roxbury Medical Association and its purpose will be to discuss certain forms of group health practice with particular reference to the manner in which such practice may affect the membership of the Norfolk District Medical Society.

Members of the Norfolk District Medical Society who may be interested in the subject are invited to attend and to present their views for the information of the councilors.

ESSEX NORTH DISTRICT MEDICAL SOCIETY

The ninety-ninth semi-annual meeting of the Essex North District Medical Society will be a combined meeting with Essex South District Medical Society and will

held at the Danvers State Hospital on Wednesday
ary 3

PROGRAM

- 00-5:00 p.m. Ward visits.
- 00-7:00 p.m. Clinic.
- 00 p.m. Dinner Dr John S. Hodgson will speak
on "Head Injuries."

TED STATES MARINE HOSPITAL

The staff meeting of the United States Marine Hospital
Chelsea will be held at "The Hut," on Friday after
4, January 12 at 4:00 Dr Leroy A. Schall will talk,
subject being "Acute Infections of the Upper Respira-
Tract."

JOHN W. TRASK, *Medical Director in Charge*

AMERICAN SCIENTIFIC CONGRESS

The Eighth American Scientific Congress will be held
Washington District of Columbia, from May 10 to 18
in the auspices of the Government of the United
States of America.

In pursuance of a special act of the Congress of the United
States invitations on behalf of the President have been
extended to the governments of the American republics
are members of the Pan American Union to participate
in the forthcoming meeting. Scientific institutions and
organizations are also cordially invited to send representa-

On April 14 the Pan American Union will celebrate
fiftieth anniversary of its founding. Although the
Congress will convene a few weeks subsequent to the
anniversary date, it will be one of the important phases
of that notable celebration. It is hoped that the presence
of Washington of many distinguished scientists of all the
American republics as participants in this congress will
be as one of the many tributes to the Pan American
Union on the occasion of celebrating the completion of
half a century of invaluable service in the fostering of
friendship and better understanding among the repub-
lics of the Western Hemisphere.

It has been decided that the congress will be divided
into the following sections, each to be in charge of a
committee assisted by a vice-chairman, secretary and sec-
retary: anthropological sciences biological sci-
ences geological sciences agriculture and conservation
public health and medicine physical and chemical sci-
ences statistics history and geography international law,
politics and jurisprudence economics and sociology
education.

The chairmen of the respective sections will be selected
as early as date, after which the detailed agenda of each
section will be announced.

In accordance with established precedent at inter-
national conferences, the official languages of the con-
gress will be English Spanish, Portuguese and French.
Papers may be submitted in any one of the official lan-
guages and appropriate arrangements will be made for
presentation of the papers or résumés thereof in the
other official languages of the congress.

The Government of the United States of America at-
taches particular significance to the forthcoming congress
an important factor in the promotion of co-operative
action among the governments and peoples of the Amer-
icas. It is sincerely hoped that prominent scientists
throughout the continent may be in a position to contrib-
ute to the achievements of the congress by bringing to the
sessions the wealth of their knowledge and experience,
while enjoying the opportunity of renewing old and mak-
ing new friendships among the other delegates present
at this occasion.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY JANUARY 1

THURSDAY JANUARY 2

- 9-10 a.m. Thirty Years Experience in the Treatment of Fractures.
Dr John D. Adams. Joseph H. Pratt Diagnostic Hospital.
- 10 a.m.-12:30 p.m. Boston Dispensary tumor clinic.
- 8:15 p.m. Greater Boston Medical Society Auditorium, Beth Israel
Hospital.

WEDNESDAY JANUARY 3

- 9-10 a.m. Hospital case presentation. Dr S. J. Thannhauser
Joseph H. Pratt Diagnostic Hospital.
- 12 m. Clinicopathological conference. Children's Hospital amphitheater.
- 12 m. Norfolk District Medical Society Boston Medical Library
8 Faneuil Boston.
- 2 p.m.-4 p.m. Joint medical and surgical clinic. Peter Bent Brigham
Hospital.

THURSDAY JANUARY 4

- 8:30 a.m.-9:30 a.m. Combined clinic of the medical, surgical, ortho-
pedic and pediatric services of the Children's Hospital and the
Peter Bent Brigham Hospital at the Children's Hospital.
- 9-10 a.m. Estrogen and Androgen Assay. Indications and Interpretations.
Dr H. T. Wertheim and Dr C. H. Lawrence. Joseph H.
Pratt Diagnostic Hospital.
- 5 p.m. Fulkner Hospital clinicopathological conference.

FRIEDAY JANUARY 5

- 9-10 a.m. The Treatment of Epilepsy by Phenytoin and Dilantin
Sodium and by Various Sympathetic Drug Combinations. Dr Ben-
jamin Cohen. Joseph H. Pratt Diagnostic Hospital.
- 10 a.m.-12:30 p.m. Boston Dispensary tumor clinic.
- 12 m. Clinical meeting of the Children's Medical Service Massachu-
setts General Hospital. Ether Dome.
- 12 m. Urological conference. Massachusetts General Hospital
lower amphitheater. Out Patient Department.

SATURDAY JANUARY 6

- 9-10 m. Hospital case presentation. Dr S. J. Thannhauser
Joseph H. Pratt Diagnostic Hospital.
- 10 a.m.-12 m. Medical staff round of the Peter Bent Brigham Hos-
pital. Conducted by Dr. Soren Weiss.

SUNDAY JANUARY 7

- 4 p.m. Digestion and Indigestion. Dr Chester M. Jones. Free public
lecture. Harvard Medical School, amphitheater of Building D.

*Open to the medical profession.

- DECEMBER 29 and 30 — Phi Delta Epsilon. Page 918, issue of December 7
- JANUARY 2 — Greater Boston Medical Society. Page 1041
- JANUARY 2-23 — Joseph H. Pratt Diagnostic Hospital, Medical Conference
Program. Page 1041
- JANUARY 3 — Metropolitan State Hospital. Clinicopathological conference.
Page 1001 issue of December 21
- JANUARY 4 — Faulkner Hospital. Clinicopathological conference. Page
1042.
- JANUARY 3 — Peter Bent Brigham Hospital. Joint medical and surgical
clinic. Page 1042.
- JANUARY 4 — Combined clinic of the medical, surgical, orthopedic and
pediatric services of the Children's Hospital and the Peter Bent Brigham
Hospital. Page 1042
- JANUARY 5 — United States Marine Hospital. Page 1001 issue of Decem-
ber 21
- JANUARY 6, 7, 8, 9, 10 — American Board of Obstetrics and Gynecology
Page 160 issue of 11 by 27 and page 778 issue of November 15.
- JANUARY 10-February 27 — Salem Hospital Public Health Lectures. Page
1042
- JANUARY 10 — Free Public Lectures, Harvard Medical School.
Page 1042.
- JANUARY 11 — Penitentiary Association of Physicians. 8:30 p.m. Hotel
Bartlett, Harvard Hill
- JANUARY 12 — United States Marine Hospital. Note above.
- JANUARY 13 and 22 — Cutter Lectures. Page 1042.
- JANUARY 23 — American Academy of Orthopaedic Surgeons. 11 and
12 p.m. Boston.
- JANUARY 24-25 — International College of Surgeons. Page 77 issue
of November 9
- JANUARY 26-27 — American Orthopaedic Association. Page 95
issue of December 11
- JANUARY 28, 29 and 30 — American Board of Ophthalmology. Page 79
issue of November 2.
- MARCH 7-9 — The New England Hospital Association. Hotel Statler
Boston.
- MAY 10-18 — American Nephrology Congress. Boston

MAY 14 — Pharmacopoeial Convention Page 894 issue of May 25
 JUNE 7-9 — American Board of Obstetrics and Gynecology Page 1019
 issue of June 15

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH

JANUARY 3 — Semi annual meeting Combined meeting with Essex South
 Danvers State Hospital Hathorne 7 p m Page 1042

ESSEX SOUTH

JANUARY 3 — Head Injuries Dr John S Hodgson Danvers State Hos-
 pital Hathorne.

FEBRUARY 14 — Cough Sputum Hemoptysis — How shall they be investi-
 gated? Dr Reeve H Betts Essex Sanatorium Middleton

MARCH 6 — Experimental and Clinical Considerations of Sulfanilamide
 Treatment of Hemolytic Streptococcal Infections Dr Champ Lyons Lynn
 Hospital Lynn

APRIL 3 — Addison Gilbert Hospital Gloucester

MAY 8 — Annual meeting Salem Country Club Peabody

HAMPSHIRE

JANUARY 10

MARCH 13

MAY 8

All meetings are held at 11 30 a m at the Cooley Dickinson Hospital,
 Northampton

MIDDLESEX EAST

JANUARY 10

MARCH 20

MAY 15

Meetings are held at 12:15 p m at the Unicorn Country Club Stoneham

MIDDLESEX NORTH

JANUARY 31

APRIL 24

JULY 31

OCTOBER 30

NORFOLK

JANUARY 3 — Page 1042

NORFOLK SOUTH

JANUARY 4

FEBRUARY 1

MARCH 7

APRIL 4

MAY 2

All meetings with the exception of one which is usually held at the
 Quincy City Hospital are held at the Norfolk County Hospital in South
 Braintree at 12 o'clock noon

PLYMOUTH

JANUARY 18 — Brockton Hospital Brockton

MARCH 21 — Goddard Hospital Brockton

APRIL 18 — State Farm

MAY 16 — Lakeville Sanatorium Lakeville

SUFFOLK

JANUARY 31 — Scientific meeting Subject to be announced later

MARCH 27 — Scientific meeting Symposium on Ulcerative Colitis and
 Diarrheas Under the direction of Dr Chester M Jones

APRIL 24 — Annual meeting in conjunction with the Boston Medical
 Library Election of officers Program and speakers to be announced later

WORCESTER

JANUARY 10 — Worcester City Hospital

FEBRUARY 14 — Worcester State Hospital

MARCH 13 — Worcester Memorial Hospital

APRIL 10 — Worcester Hahnemann Hospital

MAY 8 — Worcester Country Club

Each meeting begins with a dinner at 6 30 p m and is followed by a
 business and scientific meeting

BOOK REVIEWS

*Pneumonia With special reference to pneumococcus lobar
 pneumonia* Roderick Heffron. 1086 pp New
 York The Commonwealth Fund, 1939 \$4.50

Everyone knows that pneumonia is as important an in-
 fection as there is costly, of high mortality, and yet be-
 coming increasingly amenable to treatment as more is

learned of the disease and its peculiarities The ordinary
 medical textbook does the best it can to describe the treat-
 ment of pneumococcal infection It is a difficult matter,
 however, to do justice to so important a subject in thirty
 or forty pages and thus is about the amount of space usual
 ly allotted

Dr Heffron's book is an admirable piece of work,
 done with painstaking thoroughness The fact that there
 are 1471 references cited in the bibliography is an indica-
 tion of how carefully the work of other investigators has
 been considered. And, of course, Dr Heffron's own con-
 tributions to the pneumonia problem in Massachusetts
 are well known not only in New England but all over the
 United States

The book is well written and well printed The illus-
 trations and tables are easily understandable. The ar-
 rangement of the contents is excellent one easily can find
 in the text anything about pneumonia from a description
 of abortive pneumonia at the beginning of the alphabet
 to x ray treatment of pneumonia at the end The clinical
 aspects of pneumonia, its bacteriology, how immunity is
 established, what can be done to prevent pneumonia, all
 receive due consideration The treatment of pneumonia
 with serum, vaccine and chemicals is discussed most thor-
 oughly, including nicely written descriptions of how to
 do things for example, the best technic for typing, for
 the administration of serum or for the use of sulfanilamide
 and allied agents

In the preface Dr Heffron states that this book was
 written to present a comprehensive discussion of pneu-
 monia with special reference to pneumococcal lobar pneu-
 monia and measures for its treatment. He has accom-
 plished his purpose most skilfully Hospital and medical
 school libraries will wish to have a copy of this book for
 reference. Doctors and medical students will wish to own
 it, because it tells so clearly what to do for the individual
 patient ill with pneumonia or any of its complications

Sketches in Psychosomatic Medicine Nervous and Men-
 tal Disease Monograph No 65 Smith E. Jelliffe.
 155 pp New York Nervous and Mental Disease
 Publishing Company, 1939 \$3.00

All the papers in this book have previously appeared in
 medical journals They now are produced in a conven-
 ient form as a brief monograph The entire series is de-
 voted to the exposition of the Freudian explanation of
 certain bodily signs and the effect of the emotions on
 physical symptoms The author is a sound devotee of
 psychoanalysis and places his material before the medical
 profession in an expert manner The book should be
 widely read for it is a clear presentation of the psycho-
 analytical viewpoint. References are given to the impor-
 tant literature There are a few diagrams as illustrations,
 and the book has an index. Perhaps the most important
 paper in the whole book is that on the bodily organs in
 psychopathology, in which the author summarizes his
 views on the subject.

ERRATUM

Due to a misplaced slug, the last line in Dr Thomas
 B Quigley's article, 'Biliary Surgery in the Aged,' on
 page 974 of the December 21 issue of the *Journal* is in-
 correct. It should read 'biliary disease is discussed'.
 On request, the *Journal* will forward a slip with the cor-
 rect line for inserting or pasting in the bound volume.
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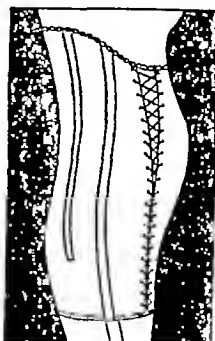
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C. — Correspondence
C. R. — Case Record
E. — Editorial
M. M. S. — Massachusetts Medical Society
M. P. — Medical Progress
M. R. — Meeting Report
Misc. — Miscellaneous

N — Notice
N. M. S. M. — New England Medical Society of Massachusetts
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Or — Original Article
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ANTEMORTEM AND POSTMORTEM RECORDS AS USED
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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